```
Welcome to STN International!  Enter x:x

LOGINID:ssspta1612bxr

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  AUG 15  CAOLD to be discontinued on December 31, 2008
 NEWS  3  OCT 07  EPFULL enhanced with full implementation of EPC2000
 NEWS  4  OCT 07  Multiple databases enhanced for more flexible patent
                  number searching
 NEWS  5  OCT 22  Current-awareness alert (SDI) setup and editing
                  enhanced
 NEWS  6  OCT 22  WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT
                  Applications
 NEWS  7  OCT 24  CHEMLIST enhanced with intermediate list of
                  pre-registered REACH substances
 NEWS  8  NOV 21  CAS patent coverage to include exemplified prophetic
                  substances identified in English-, French-, German-,
                  and Japanese-language basic patents from 2004-present
 NEWS  9  NOV 26  MARPAT enhanced with FSORT command
 NEWS 10  NOV 26  MEDLINE year-end processing temporarily halts
                  availability of new fully-indexed citations
 NEWS 11  NOV 26  CHEMSAFE now available on STN Easy
 NEWS 12  NOV 26  Two new SET commands increase convenience of STN
                  searching
 NEWS 13  DEC 01  ChemPort single article sales feature unavailable
 NEWS 14  DEC 12  GBFULL now offers single source for full-text
                  coverage of complete UK patent families
 NEWS 15  DEC 17  Fifty-one pharmaceutical ingredients added to PS

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:34:32 ON 05 JAN 2009



Updated Search
```

=> FILE REG
COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION
FULL ESTIMATED COST | 0.22 | 0.22

FILE 'REGISTRY' ENTERED AT 13:34:43 ON 05 JAN 2009

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 JAN 2009 HIGHEST RN 1092523-63-1
DICTIONARY FILE UPDATES: 4 JAN 2009 HIGHEST RN 1092523-63-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

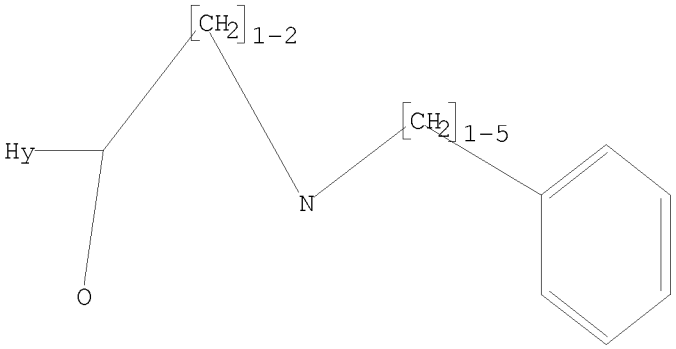
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Documents and Settings\brobinson1\My Documents\294A.str

L1 STRUCTURE UPLOADED

=> D L1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> S L1

Updated Search

```
SAMPLE SEARCH INITIATED 13:37:40 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   189391 TO ITERATE

  1.1% PROCESSED     2000 ITERATIONS                                0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:      3762194 TO  3813446
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=>
Uploading C:\Documents and Settings\brobinson1\My Documents\areareawra.str

L3      STRUCTURE UPLOADED

=> s l3
SAMPLE SEARCH INITIATED 13:38:56 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    16978 TO ITERATE

 11.8% PROCESSED     2000 ITERATIONS                               10 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       331755 TO   347365
PROJECTED ANSWERS:            1145 TO     2249

L4           10 SEA SSS SAM L3

=> s l3 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 185.40 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 13:39:00 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   339895 TO ITERATE

100.0% PROCESSED   339895 ITERATIONS                            1359 ANSWERS
SEARCH TIME: 00.00.06

L5         1359 SEA SSS FUL L3

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               188.76     188.98

FILE 'HCAPLUS' ENTERED AT 13:39:09 ON 05 JAN 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available



Updated Search
```

for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 5 Jan 2009 VOL 150 ISS 2
FILE LAST UPDATED: 4 Jan 2009 (20090104/ED)

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l5
L6 112 L5

=> s l6 and pd < autust 2003
DATE SPECIFICATION IS NOT VALID
Date specifications may use ranges and numeric operators. The date itself can be in any of the following general formats:

STN Format:	YYYYMMDD	
Slash Format:	MM/DD/YYYY or MM/YYYY	
Dot Format:	DD.MM.YYYY or MM.YYYY	
Text Format:	February 10, 1987	Feb 1989
	Feb. 10, 1987	1990
	Feb. 10, 2000	1998 - 2001
	Feb 10, 1987	July 1997 - May 2002
	10 February 1987	March 5 - 8, 1990
	10 Feb 2007	April - June, 1999

Any year entered with only two digits will be interpreted as being in the range 1900-1999. Thus, Mar 12 01 will be searched as 19010312.

=> s l6 and pd < august 2002
22821027 PD < AUGUST 2002
(PD<20020800)
L7 61 L6 AND PD < AUGUST 2002

=> s l6 and rode, b?/au
412 RODE, B?/AU
L8 1 L6 AND RODE, B?/AU

=> d l8, ibib abs hitstr, 1

L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:60474 HCAPLUS
DOCUMENT NUMBER: 140:128278

Updated Search

TITLE: Preparation of 1-pyridyl-2-[(2-phenylethyl)amino]ethanols as inhibitors of cholesterol biosynthesis

INVENTOR(S): Rode, Breda; Rozman, Damjana; Fon, Tacer Klementina; Kocjan, Darko

PATENT ASSIGNEE(S): Lek Pharmaceuticals D.D., Slovenia

SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007456	A1	20040122	WO 2003-SI21	20030709
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21268	A	20040229	SI 2002-177	20020717
SI 21368	A	20040630	SI 2002-287	20021128
CA 2493004	A1	20040122	CA 2003-2493004	20030709
AU 2003248614	A1	20040202	AU 2003-248614	20030709
AU 2003248614	B2	20070830		
EP 1546105	A1	20050629	EP 2003-764285	20030709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012945	A	20050712	BR 2003-12945	20030709
CN 1668594	A	20050914	CN 2003-816850	20030709
CN 1297540	C	20070131		
JP 2005538081	T	20051215	JP 2004-521370	20030709
NZ 537635	A	20061130	NZ 2003-537635	20030709
RU 2309949	C2	20071110	RU 2005-104420	20030709
IN 2004CN03157	A	20060303	IN 2004-CN3157	20041213
ZA 2005000122	A	20060726	ZA 2005-122	20050106
MX 2005PA00663	A	20050920	MX 2005-PA663	20050114
NO 2005000833	A	20050418	NO 2005-833	20050216
US 20050256172	A1	20051117	US 2005-521294	20050524

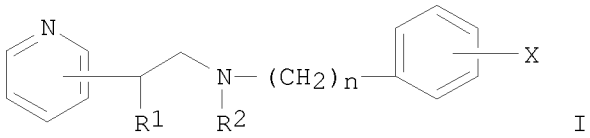
PRIORITY APPLN. INFO.:

SI 2002-177	A	20020717
SI 2002-287	A	20021128
WO 2003-SI21	W	20030709

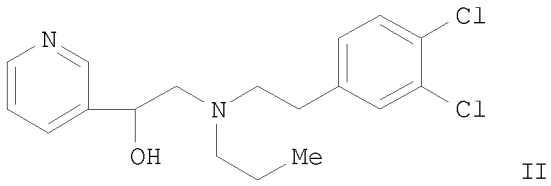
OTHER SOURCE(S): MARPAT 140:128278

GI

Updated Search



I



II

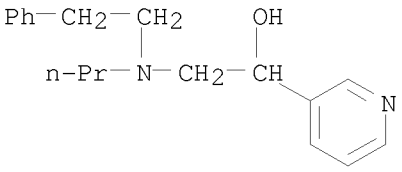
AB Title compds. I [wherein n = 1-4; R1 = H, OH, or alkoxy; R2 = H or alkyl; X = H, F, Cl, Br, OH, CF3, 3,4-Cl2, 2,4-Cl2, or alkoxy; and the enantiomers, diastereoisomers, racemates, or physiol. acceptable acid addition salts thereof] were prepared as ligands of σ receptors for inhibiting cholesterol biosynthesis. For example, reaction of 3-(bromoacetyl)pyridine•HBr with NaBH4 in absolute EtOH, followed by alkylation with PrNH2 afforded 1-(3-pyridyl)-2-propylaminoethanol (50%). The amine was coupled with 3,4-dichlorophenylacetic acid in CH2Cl2 in the presence of DCC to give 1-(3-pyridyl)-2-[N-[2-(3,4-dichlorophenyl)acetyl]-N-propylamino]ethanol (50%). Reduction of the acetamide using LiAlH4 in anhydrous THF provided the ethylamine (60%), which was converted to II•2HBr (BK-35•2HBr) in 85% yield. The latter completely blocked cholesterol biosynthesis and showed a ten-fold increase in the accumulation of sterol intermediates of the postsqualene portion of cholesterol biosynthesis. Thus, I and their pharmaceutical compns. are appropriate for the treatment of hypercholesterolemia and hyperlipemia in humans (no data).

IT 648930-50-1P, 1-(3-Pyridyl)-2-[N-(2-phenylethyl)-N-propylamino]ethanol 648930-51-2P, 1-(3-Pyridyl)-2-[N-(2-phenylethyl)-N-propylamino]ethanol dihydrobromide 648930-53-4P, 1-(3-Pyridyl)-2-[N-[2-(3,4-dichlorophenyl)ethyl]-N-methylamino]ethanol 648930-54-5P, 1-(3-Pyridyl)-2-[N-[2-(3,4-dichlorophenyl)ethyl]-N-methylamino]ethanol dihydrobromide 648930-55-6P, 1-(3-Pyridyl)-2-[N-[2-(3,4-dichlorophenyl)ethyl]-N-propylamino]ethanol 648930-56-7P, 1-(3-Pyridyl)-2-[N-[2-(3,4-dichlorophenyl)ethyl]-N-propylamino]ethanol dihydrobromide 648930-57-8P, 1-(4-Pyridyl)-2-[N-[2-(3,4-dichlorophenyl)ethyl]-N-methylamino]ethanol 648930-58-9P, 1-(4-Pyridyl)-2-[N-[2-(3,4-dichlorophenyl)ethyl]-N-methylamino]ethanol dihydrobromide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anticholesteremic agent; preparation of pyridyl(phenylethylamino)ethanols as inhibitors of cholesterol biosynthesis for treatment of hypercholesterolemia and hyperlipemia)

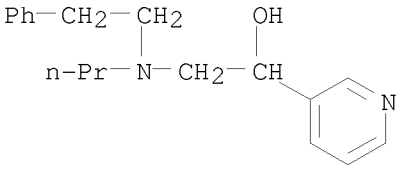
RN 648930-50-1 HCAPLUS

CN 3-Pyridinemethanol, α-[[(2-phenylethyl)propylamino]methyl]- (CA INDEX NAME)

Updated Search

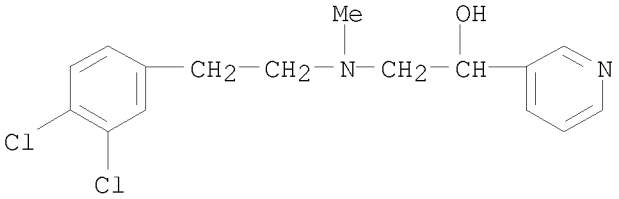


RN 648930-51-2 HCAPLUS
CN 3-Pyridinemethanol, α-[[(2-phenylethyl)propylamino]methyl]-, hydrobromide (1:2) (CA INDEX NAME)

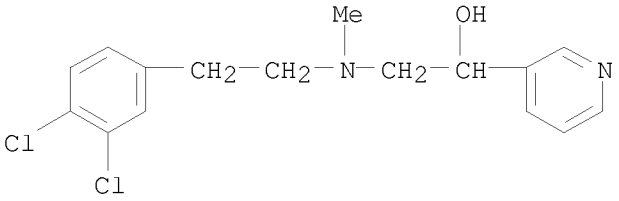


●2 HBr

RN 648930-53-4 HCAPLUS
CN 3-Pyridinemethanol, α-[[[2-(3,4-dichlorophenyl)ethyl]methylamino]methyl]- (CA INDEX NAME)



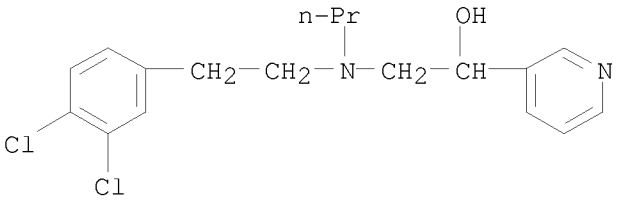
RN 648930-54-5 HCAPLUS
CN 3-Pyridinemethanol, α-[[[2-(3,4-dichlorophenyl)ethyl]methylamino]methyl]-, hydrobromide (1:2) (CA INDEX NAME)



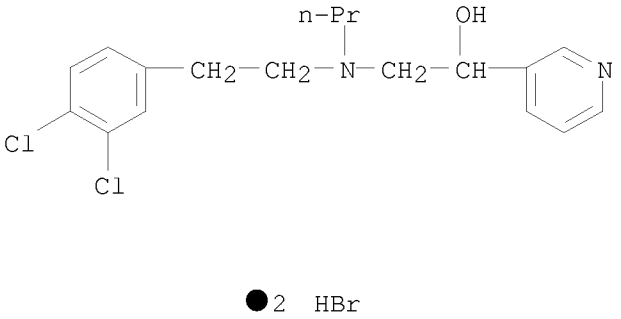
●2 HBr

Updated Search

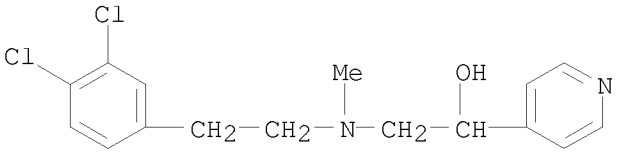
RN 648930-55-6 HCAPLUS
CN 3-Pyridinemethanol, α-[[[2-(3,4-dichlorophenyl)ethyl]propylamino]methyl]- (CA INDEX NAME)



RN 648930-56-7 HCAPLUS
CN 3-Pyridinemethanol, α-[[[2-(3,4-dichlorophenyl)ethyl]propylamino]methyl]-, hydrobromide (1:2) (CA INDEX NAME)

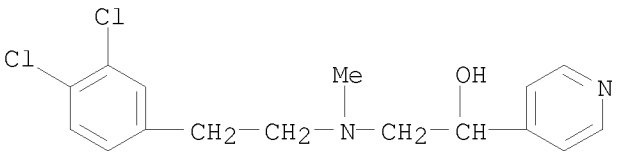


RN 648930-57-8 HCAPLUS
CN 4-Pyridinemethanol, α-[[[2-(3,4-dichlorophenyl)ethyl]methylamino]methyl]- (CA INDEX NAME)



RN 648930-58-9 HCAPLUS
CN 4-Pyridinemethanol, α-[[[2-(3,4-dichlorophenyl)ethyl]methylamino]methyl]-, hydrobromide (1:2) (CA INDEX NAME)

Updated Search



● 2 HBr

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 13:34:32 ON 05 JAN 2009)

FILE 'REGISTRY' ENTERED AT 13:34:43 ON 05 JAN 2009
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 STRUCTURE UPLOADED
L4 10 S L3
L5 1359 S L3 FULL

FILE 'HCAPLUS' ENTERED AT 13:39:09 ON 05 JAN 2009
L6 112 S L5
L7 61 S L6 AND PD < AUGUST 2002
L8 1 S L6 AND RODE, B?/AU

=> s l7 not l8
L9 61 L7 NOT L8

=> s l9 and rozman, d?/au
73 ROZMAN, D?/AU
L10 0 L9 AND ROZMAN, D?/AU

=> s l9 and fon tacer, k?/au
2 FON TACER, K?/AU
L11 0 L9 AND FON TACER, K?/AU

=> s l9 and kocjan, d?/au
73 KOCJAN, D?/AU
L12 0 L9 AND KOCJAN, D?/AU

=> d l9, ibib abs fhitstr, 1-61

L9 ANSWER 1 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:763926 HCAPLUS
DOCUMENT NUMBER: 137:288901
TITLE: Effect of a 28-d treatment with L-796568, a novel β3-adrenergic receptor agonist, on energy expenditure and body composition in obese men
AUTHOR(S): Larsen, Thomas M.; Toubro, Soren; van Baak, Marleen A.; Gottesdiener, Keith M.; Larson, Patrick; Saris, Wim H. M.; Astrup, Arne

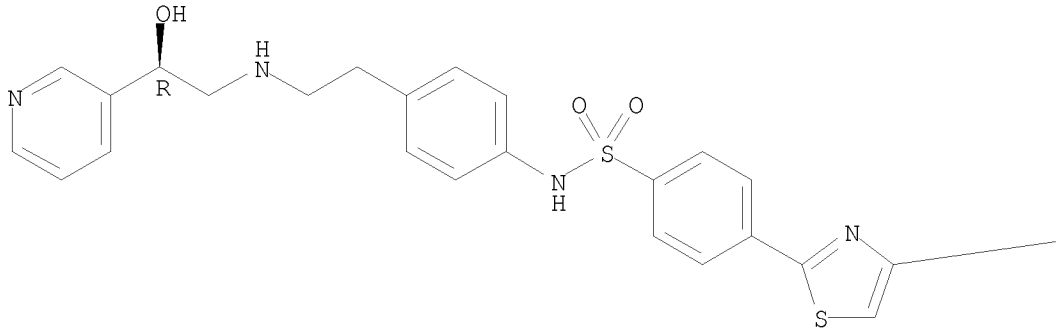
Updated Search

CORPORATE SOURCE: Research Department of Human Nutrition, The Royal Veterinary and Agricultural University, Copenhagen, Den.
SOURCE: American Journal of Clinical Nutrition (2002), 76(4), 780-788
CODEN: AJCNAC; ISSN: 0002-9165
PUBLISHER: American Society for Clinical Nutrition
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Stimulation of energy expenditure (EE) with selective thermogenic β-adrenergic agonists may be a promising approach for treating obesity. We analyzed the effects of the highly selective human β3-adrenergic agonist L-796568 on 24-h EE, substrate oxidation, and body composition in obese, weight-stable men. In this 2-center, double-blind, randomized, parallel-group study, we measured 24-h EE before and after 28 d of treatment with L-796568 (375 mg/d) or placebo during weight maintenance (ie, without dietary intervention) in nondiabetic, nonsmoking men aged 25-49 yr with body mass index (in kg/m2) of 28-35 (n = 10 subjects per treatment group). The mean change in 24-h EE from before to after treatment did not differ significantly between groups (92±586 and 86±512 kJ/24 h for the L-796568 and placebo groups, resp.). The change in 24-h nonprotein RQ from before to after treatment did not differ significantly between groups (0.009±0.021 and 0.009±0.029, resp.). No changes in glucose tolerance were observed, but triacylglycerol concns. decreased significantly with L-796568 treatment compared with placebo (-0.76±0.76 and 0.42±0.31 mmol/L, resp.; P < 0.002). Overall, treatment-related changes in body composition were not observed, but higher plasma L-796568 concns. in the L-796568 group were associated with greater decreases in fat mass (r = -0.69, P < 0.03). Treatment with L-796568 for 28 d had no major lipolytic or thermogenic effect but it lowered triacylglycerol concns. This lack of chronic effect on energy balance is likely explained by insufficient recruitment of β3-responsive tissues in humans, down-regulation of the β3-adrenergic receptor-mediated effects with chronic dosing, or both.
IT 211031-81-1, L-796568
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of a 28-d treatment with L-796568, a novel β3-adrenergic receptor agonist, on energy expenditure and body composition in obese men)
RN 211031-81-1 HCAPLUS
CN Benzenesulfonamide, N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[4-[4-(trifluoromethyl)phenyl]-2-thiazolyl]-, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry.

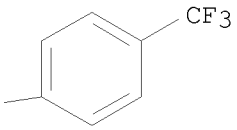
Updated Search

PAGE 1-A



●2 HCl

PAGE 1-B



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:505889 HCAPLUS
DOCUMENT NUMBER: 138:49354
TITLE: Metabolism of a thiazole benzenesulfonamide derivative, a potent and selective agonist of the human β3-adrenergic receptor, in rats: identification of a novel isethionic acid conjugate
AUTHOR(S): Tang, Wei; Stearns, Ralph A.; Miller, Randall R.; Ngui, Jason S.; Mathvink, Robert J.; Weber, Ann E.; Kwei, Gloria Y.; Strauss, John R.; Keohane, Carol A.; Doss, George A.; Chiu, Shuet-Hing L.; Baillie, Thomas A.
CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ, USA
SOURCE: Drug Metabolism and Disposition (2002), 30(7), 778-787
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal

Updated Search

LANGUAGE: English

AB (R)-N-[4-[2-[[2-Hydroxy-2-(pyridin-3-yl)ethyl]amino]ethyl]phenyl]-4-[4-(4-trifluoro-methylphenyl)thiazol-2-yl]benzenesulfonamide (1) is a potent and selective agonist of the human β3-adrenergic receptor. We report herein the data from studies of the metabolism and excretion of 1 in rats. Five metabolites were identified in the bile of male Sprague-Dawley rats administered 3H-labeled 1 by either oral gavage (10 mg/kg) or i.v. injection (3 mg/kg). These included a pyridine N-oxide derivative (M2), a primary amine resulting from N-dealkylation and loss of the pyridinyl-2-hydroxyethyl group (M4), a carboxylic acid derived from N-dealkylation and loss of the pyridyl-2-hydroxyethyl amine (M5), and the corresponding taurine and isethionic acid conjugates (M1 and M3). Metabolites M1 and M3 also were identified in rats treated with M5 and were generated in incubations of M5 with rat liver subcellular fractions in the presence of ATP and CoA with supplementary taurine or isethionic acid. These results suggest that M5 is the precursor of M1 and M3 and that the formation of these conjugated metabolites follows similar mechanisms of amino acid conjugation. On the other hand, M2, M4, and M5 were produced from 1 in an NADPH-dependent manner in incubations with liver microsomes from rats, dogs, monkeys, and humans. In human liver prepns., these routes of biotransformation were shown to be catalyzed by cytochrome P 450 3A4. In a bidirectional transport assay, transport of 1 across a monolayer of cells expressing P-glycoprotein (Pgp) was observed to be similar to that of vinblastine, which is an established substrate of the transporter protein: This finding, together with the observation that the parent compound was excreted in the feces of bile duct-cannulated animals following i.v. dosing, suggests that 1 is subject to Pgp-mediated excretion from intestine of rats.

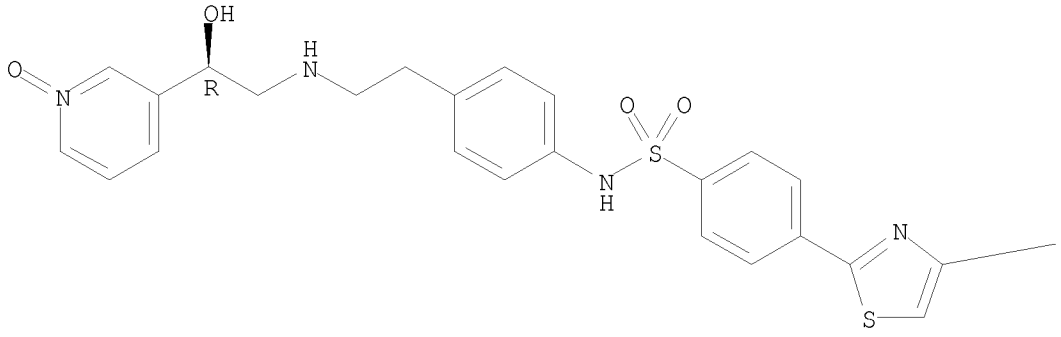
IT 479249-38-2P
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(metabolism of a thiazole benzenesulfonamide derivative, a potent and selective agonist of human β3-adrenergic receptor, in rats)

RN 479249-38-2 HCAPLUS

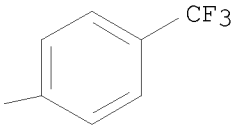
CN Benzenesulfonamide, N-[4-[2-[[(2R)-2-hydroxy-2-(1-oxido-3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[4-[4-(trifluoromethyl)phenyl]-2-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



Updated Search



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:505888 HCAPLUS
DOCUMENT NUMBER: 138:49353
TITLE: The pharmacokinetics of a thiazole benzenesulfonamide β3-adrenergic receptor agonist and its analogs in rats, dogs, and monkeys: improving oral bioavailability
AUTHOR(S): Stearns, Ralph A.; Miller, Randy R.; Tang, Wei; Kwei, Gloria Y.; Tang, Frank S.; Mathvink, Robert J.; Naylor, Elizabeth M.; Chitty, Dawn; Colandrea, Vincent J.; Weber, Ann E.; Colletti, Adria E.; Strauss, John R.; Keohane, Carol Ann; Feeney, William P.; Iliff, Susan A.; Chiu, Shuet-Hing Lee
CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ, USA
SOURCE: Drug Metabolism and Disposition (2002), 30(7), 771-777
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pharmacokinetics and oral bioavailability of (R)-N-[4-[2-[[2-hydroxy-2-(pyridin-3-yl)ethyl]amino]ethyl]phenyl]-4-[4-[4-(trifluoromethylphenyl)]thiazol-2-yl]benzenesulfonamide (1), a 3-pyridyl thiazole benzenesulfonamide β3-adrenergic receptor agonist, were investigated in rats, dogs, and monkeys. Systemic clearance was higher in rats (.apprx.30 mL/min/kg) than in dogs and monkeys (both .apprx.10 mL/min/kg), and oral bioavailability was 17, 27, and 4%, resp. Since systemic clearance was 25 to 40% of hepatic blood flow in these species, hepatic extraction was expected to be low, and it was likely that oral bioavailability was limited either by absorption or a large first-pass effect in the gut. The absorption and excretion of 3H-labeled 1 were investigated in rats, and only 28% of the administered radioactivity was orally absorbed. Subsequently, the hepatic extraction of 1 was evaluated in rats (30%) and monkeys (47%). The low oral bioavailability in rats could be explained completely by poor oral absorption and hepatic first-pass metabolism; in monkeys, oral absorption was either less than in rats or first-pass extraction in the gut was greater. In an attempt to increase oral exposure, the pharmacokinetics and oral bioavailability of two potential prodrugs of 1, an N-Et [(R)-N-[4-[2-[ethyl[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[4-[4-

(trifluoromethyl)phenyl]thiazol-2-yl]benzenesulfonamide; 2] and a morpholine derivative [(R)-N-[4-[2-[2-(3-pyridinyl)morpholin-4-yl]ethyl]phenyl]-4-[4-[4-(t rifluoromethyl)phenyl]thiazol-2-yl]benzenesulfonamide; 3], were evaluated in monkeys. Conversion to 1 was low (<3%) with both derivs., and neither entity was an effective prodrug, but the oral bioavailability of 3 (56%) compared with 1 (4%) was significantly improved. The hypothesis that the increased oral bioavailability of 3 was due to a reduction in hydrogen bonding sites in the mol. led to the design of (R)-N-[4-[2-[[2-hydroxy-2-(pyridin-2-yl)ethyl]amino]ethyl]phenyl]-4-[4-(4-trifluoromethylphenyl)thiazol-2-yl]benzenesulfonamide (4), a 2-pyridyl β3-adrenergic receptor agonist with improved oral bioavailability in rats and monkeys.

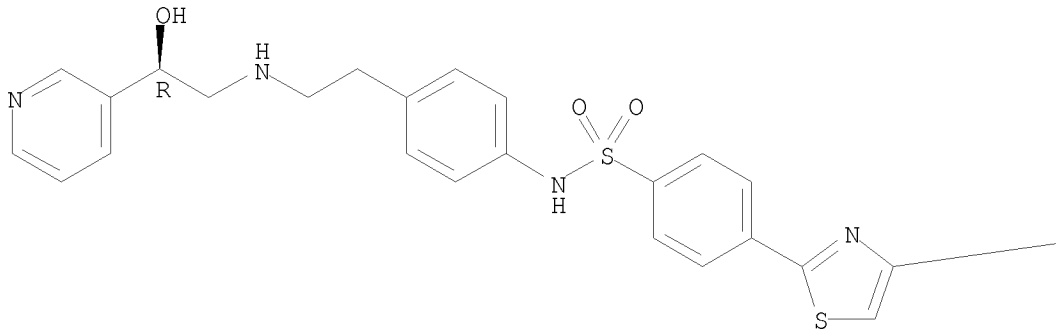
IT 211031-01-5
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(pharmacokinetics of a thiazole benzenesulfonamide β3-adrenergic receptor agonist and its analogs in rats, dogs, and monkeys)

RN 211031-01-5 HCAPLUS

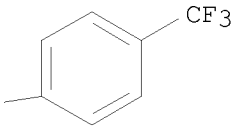
CN Benzenesulfonamide, N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[4-[4-(trifluoromethyl)phenyl]-2-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:483565 HCAPLUS

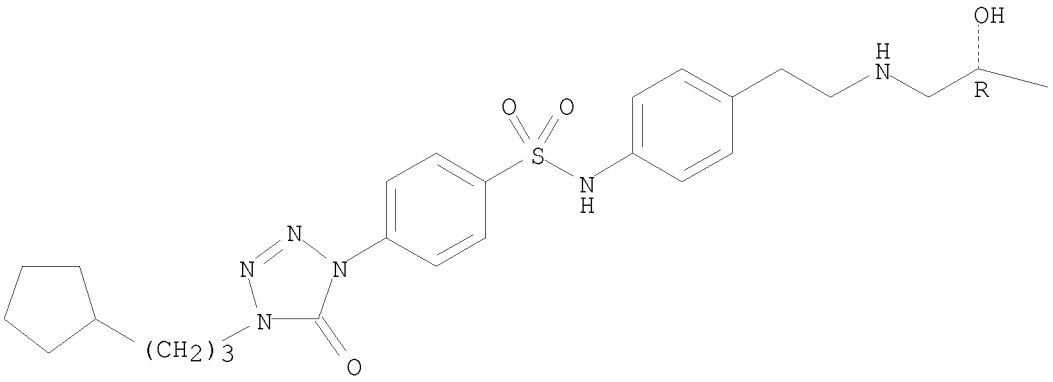
Updated Search

DOCUMENT NUMBER: 137:345545
TITLE: Rapid pharmacokinetic screening for the selection of new drug discovery candidates [by] using a generic isocratic liquid chromatography-atmospheric pressure ionization tandem mass spectrometry method
AUTHOR(S): Colwell, Lawrence F., Jr.; Tamvakopoulos, Constantin S.; Wang, Pei Ran; Pivnichny, James V.; Shih, Thomas L.
CORPORATE SOURCE: Department of Basic Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2002), 772(1), 89-98
CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A generic title method was developed for the determination of plasma concns. of compds. for the selection of potential new drug discovery candidates. A 4.6 + 50-mm cyano phase column eluted with an MeCN/H2O mobile phase containing 20 mM NH4OAc and 0.4% F3CCO2H produced retention times of ≤1 min for 7 compds. possessing a wide range of structures (determined in pure aqueous solns.). This is a great advantage in new drug discovery, where many compds. are analyzed once and eliminated. No time is consumed in developing chromatog. conditions for each new compound The mass spectrometer can be optimized and the samples can be processed and analyzed all in the same day. Multiple assays can be run consecutively without changing the column or mobile phase between assays. Determination of the β3-adrenergic agonist L-770,644 in dog plasma was carried out as an example of use for pharmacokinetic screening.
IT 173901-95-6, L 770644
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(pharmacokinetic screening for the selection of new drug discovery candidates by liquid chromatog.-atmospheric pressure ionization tandem mass spectrometry, exemplified by the determination of)
RN 173901-95-6 HCAPLUS
CN Benzenesulfonamide, 4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

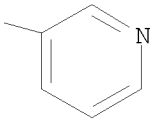
Absolute stereochemistry.

Updated Search

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:363839 HCAPLUS
DOCUMENT NUMBER: 137:15695
TITLE: Acute effect of L-796568, a novel β3-adrenergic receptor agonist, on energy expenditure in obese men
AUTHOR(S): Van Baak, Marleen A.; Hul, Gabby B. J.; Toubro, Soren; Astrup, Arne; Gottesdiener, Keith M.; DeSmet, Marina; Saris, Wim H. M.
CORPORATE SOURCE: Nutrition and Toxicology Research Institute (NUTRIM), Maastricht University, Maastricht, 6200 MD, Neth.
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (2002), 71(4), 272-279
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Our objective was to investigate the thermogenic efficacy of single oral doses of the novel β3-adrenergic receptor agonist L-796568 [(R)-N-[4-[2-[[2-hydroxy-2-(3-pyridinyl) ethyl]amino]ethyl]-phenyl] -4-[4-[4-(trifluoromethyl)phenyl] thiazol-2-yl]-benzenesulfonamide, dihydrochloride] in humans. Twelve healthy overweight to obese men participated in this 2-center, 3-period, randomized, placebo-controlled, crossover trial. In each period subjects received 250 mg L-796568, 1000 mg L-796568, or placebo. Energy expenditure and RQ were determined by indirect calorimetry; blood samples were taken; and ear temperature, heart rate, and blood pressure were measured at baseline and during the 4-h period after administration. Energy expenditure increased significantly after the

1000-mg dose (about 8%) and this was accompanied by an increase in plasma glycerol and free fatty acid concns. Systolic blood pressure also increased significantly. No changes in heart rate, diastolic blood pressure, ear temperature, plasma catecholamine, potassium, or leptin were found. Single-dose administration of 1000 mg of the novel β3-adrenergic receptor agonist L-796568 increased lipolysis and energy expenditure in overweight men. This is the first study to show such an effect of β3-adrenergic receptor agonists in humans without significant evidence for β2-adrenergic receptor involvement.

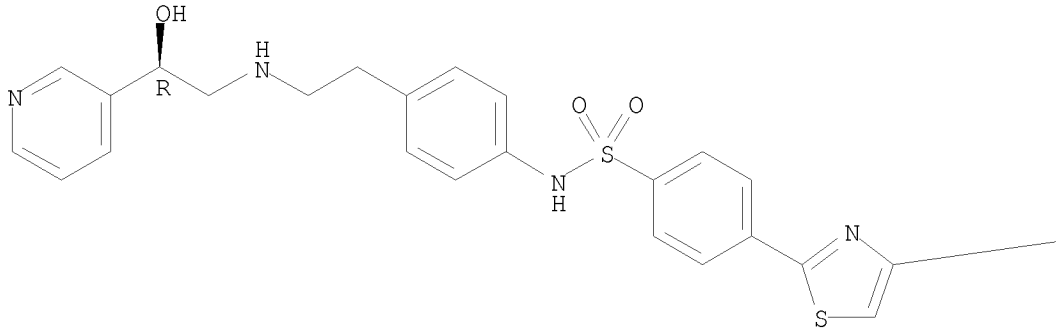
IT 211031-81-1, L 796568
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of L-796568, a novel β3-adrenergic receptor agonist, on energy expenditure in obese men)

RN 211031-81-1 HCAPLUS

CN Benzenesulfonamide, N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[4-[4-(trifluoromethyl)phenyl]-2-thiazolyl]-, hydrochloride (1:2) (CA INDEX NAME)

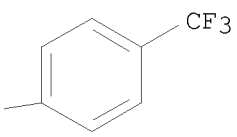
Absolute stereochemistry.

PAGE 1-A



● 2 HCl

PAGE 1-B

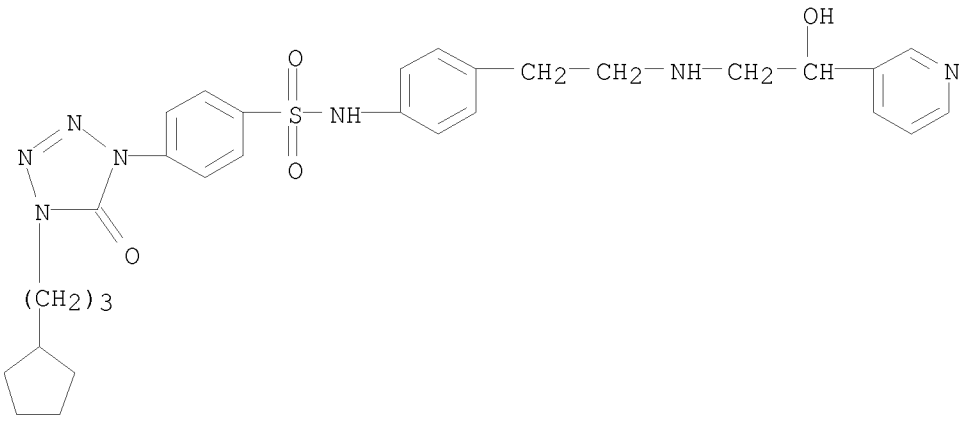


REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS

Updated Search

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:361447 HCAPLUS
DOCUMENT NUMBER: 137:175095
TITLE: Enantiomeric separation of a thiazolbenzenesulfonamide compound using packed-column subcritical fluid chromatography
AUTHOR(S): Chen, Lu; Thompson, Richard A.; Johnson, Bruce D.; Wyvratt, Jean M.
CORPORATE SOURCE: Analytical Research, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Chirality (2002), 14(5), 393-399
CODEN: CHRLEP; ISSN: 0899-0042
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Separation of enantiomers of a thiazolbenzenesulfonamide compound was performed on a Chiralpak AD column using subcrit. fluid chromatog. Effects of alc. modifier and temperature on the sepns. were studied. The results revealed that while the main adsorbing interactions were between the hydroxyl group of the analyte and the carbamate group of the stationary phase, chiral discrimination was achieved through an inclusion mechanism within the chiral cavity created along the amylose chains. Analogs and synthetic precursors of the thiazolbenzenesulfonamide studied were also investigated so as to understand the effect of functional groups and configuration of the analyte mol. upon chiral recognition.
IT 173900-99-7
RL: ANT (Analyte); ANST (Analytical study)
(enantiomeric separation of a thiazolbenzenesulfonamide compound using packed-column subcrit. fluid chromatog.)
RN 173900-99-7 HCAPLUS
CN Benzenesulfonamide, 4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

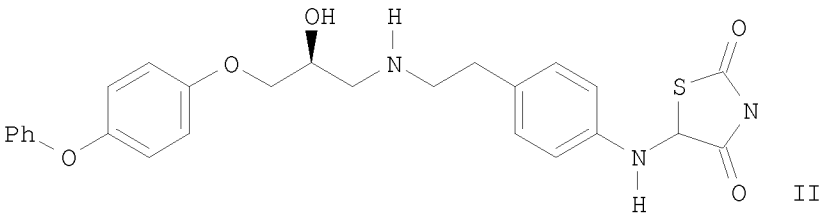
Updated Search

ACCESSION NUMBER: 2002:72073 HCAPLUS
DOCUMENT NUMBER: 136:134753
TITLE: Preparation of arylaminothizolidines and analogs as β3 adrenergic receptor agonists
INVENTOR(S): Malamas, Michael Sotirios; Largis, Elwood Eugene; Gunawan, Iwan; Li, Zenan
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006258	A1	20020124	WO 2001-US22408	20010716 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 20020032222	A1	20020314	US 2001-904161	20010712 <--
US 6465501	B2	20021015		
US 20030055079	A1	20030320	US 2002-227225	20020823
US 6569873	B2	20030527		

PRIORITY APPLN. INFO.: US 2000-218706P P 20000717
US 2001-904161 A3 20010712

OTHER SOURCE(S): MARPAT 136:134753
GI



II

AB R1Z1CH(OH)CH2NHCHR4Z2Z3NR5ZR6 [I; R1 = (un)substituted Ph, -pyridyl, etc.; R4 = H or alkyl; R5 = H, alkyl, alkoxycarbonyl, aryl, etc.; R6 = H, alkyl, aryl(alkyl); Z = e.g., 2,4-dioxothiazolidine-5,3-diyl; Z1 = bond, OCH2, SCH2; Z2 = bond, C1-6 alkyl (sic), C1-6 alkoxy (sic); Z3 = phenylene, naphthylene, benzofurylene, benzothienylene] were prepared Thus, (S)-oxiranylmethyl 3-nitrobenzenesulfonate was etherified by 4-(PhO)C6H4OH and the product aminated by 4-(H2N)C6H4CH2CH2NH2 to give, after N-protection, (S)-4-(PhO)C6H4OCH2CH(OH)CH2N(CO2CMe3)CH2CH2C6H4(NH2)-4 which was N-alkylated by 5-bromothiazolidine-2,4-dione to give, after

Updated Search

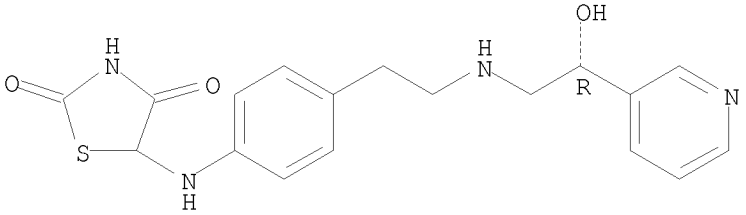
deprotection, title compound II. Data for biol. activity of I were given.

IT 321575-14-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylaminothizolidines and analogs as β3 adrenergic receptor agonists)

RN 321575-14-8 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]amino]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:740639 HCAPLUS

DOCUMENT NUMBER: 136:177412

TITLE: Liquid chromatographic-tandem mass spectrometric urine assay for a highly metabolized cyclic ureidobenzenesulfonamide: issues concerning assay specificity and quality control preparation

AUTHOR(S): Fisher, A. L.; DePuy, E.; Shih, T.; Stearns, R.; Lee, Y.; Gottesdiener, K.; Flattery, S.; De Smet, M.; Keymeulen, B.; Musson, D. G.

CORPORATE SOURCE: Merck Research Laboratories, West Point, PA, 19486, USA

SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2001), 26(5-6), 739-752
CODEN: JPBADA; ISSN: 0731-7085

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An LC-MS-MS method was validated for the quantitation of a β3 agonist (I) in human urine to support Phase I studies. I was designed to accelerate metabolism for weight reduction During assay development a significant loss of I was apparent from frozen urine quality control samples. The addition of 0.75% bovine serum albumin (BSA) in urine (volume/volume) was required to maximize the recovery of I from urine. Urine samples were basified and extracted into Me tert-Bu ether-iso-Pr alc. (90:10, volume/volume). The organic layer was washed, evaporated, reconstituted, and injected onto a 5 cm, C8 HPLC column prior to MS-MS anal. The standard curve was linear from 5 to 500 ng/mL. Intraday precision for peak area ratios from BSA urine samples at seven sep. concns. over a range of 5-500 ng/mL (n=5) was <4.0% and calculated concns. were within 91-115% of nominal concns. Interday

Updated Search

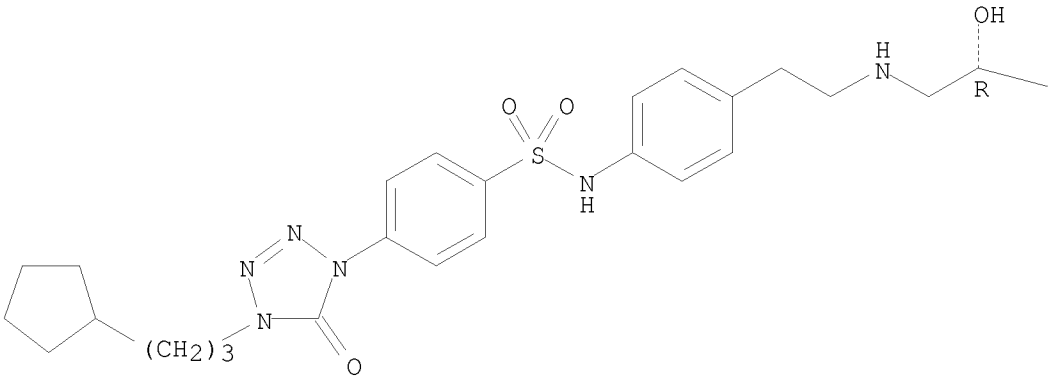
precision for BSA urine quality control (QC) samples at four sep. concns. (n=10 of each) was <5.0% and individual calculated concns. were within 90-111% of nominal concns. This work emphasizes that potential metabolites and quality control stds. should be prepared and assayed as early as possible in method development, especially before the sample collection section of the clin.
protocol is prepared The methods described here have wide utility to other compds. containing basic benzene sulfonamides and to β3 agonist candidates.

IT 173901-95-6
RL: ANT (Analyte); ANST (Analytical study)
(LC-MS-MS urine assay for a highly metabolized cyclic ureidobenzenesulfonamide and issues concerning assay specificity and quality control preparation)

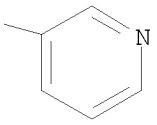
RN 173901-95-6 HCAPLUS
CN Benzenesulfonamide, 4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:729769 HCAPLUS
DOCUMENT NUMBER: 135:288694
TITLE: Processes for preparing substituted pyridines, useful as intermediates for β-adrenergic receptor agonists

Updated Search

INVENTOR(S): Dow, Robert Lee; Schneider, Steven Roy
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 57 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1138685	A2	20011004	EP 2001-302635	20010321 <--
EP 1138685	A3	20030402		
EP 1138685	B1	20040519		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 267204	T	20040615	AT 2001-302635	20010321
PT 1138685	T	20040831	PT 2001-302635	20010321
ES 2217090	T3	20041101	ES 2001-302635	20010321
TW 555761	B	20031001	TW 2001-90107208	20010327
IN 193557	A1	20040724	IN 2001-DE373	20010327
US 20020077478	A1	20020620	US 2001-820137	20010328 <--
US 6518431	B2	20030211		
ZA 2001002538	A	20020930	ZA 2001-2538	20010328
CA 2342571	A1	20010930	CA 2001-2342571	20010329 <--
BR 2001001280	A	20011106	BR 2001-1280	20010330 <--
JP 2001316393	A	20011113	JP 2001-100321	20010330 <--
HU 2001001332	A2	20021028	HU 2001-1332	20010330
HU 2001001332	A3	20040728		
RU 2223956	C2	20040220	RU 2001-108594	20010330
AU 782272	B2	20050714	AU 2001-33348	20010330
MX 2001PA03383	A	20050826	MX 2001-PA3383	20010330
CN 1320596	A	20011107	CN 2001-112348	20010402 <--
CN 1191235	C	20050302		
HK 1038019	A1	20050610	HK 2001-108923	20011220
US 20030114670	A1	20030619	US 2002-317720	20021212
US 6670480	B2	20031230		
US 20040133005	A1	20040708	US 2003-684146	20031010
US 6844441	B2	20050118		
US 20050113578	A1	20050526	US 2004-974421	20041026

PRIORITY APPLN. INFO.:
US 2000-193772P P 20000331
US 2001-820137 A3 20010328
US 2002-317720 A3 20021212
US 2003-684146 A3 20031010

OTHER SOURCE(S): CASREACT 135:288694; MARPAT 135:288694
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Several processes for preparing various pyridine derivs. are claimed. The products are used as intermediates in the synthesis of known β-adrenergic receptor agonists. In particular, the halide and sulfonate ester intermediates I are prepared, and are used in the synthesis of the amino alcs. II [wherein n = 0-3; R1 = H, halo; R2 = H, halo, CF3, cyano, SR4, OR4, SO2R4, OCOR5, (un)substituted alkyl; R3 =

Updated Search

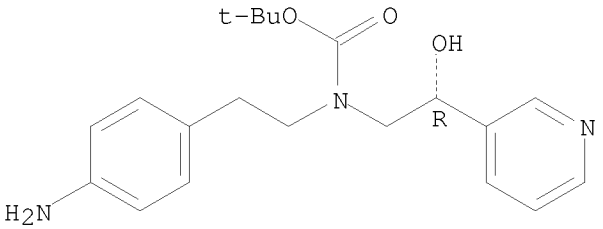
tetrahydrofuranyl, tetrahydropyranyl, or silyl protecting group; X = halo, OSO3Me, OSO2Ph, OSO2C6H4Me-p, OSO2C6H4NO2-m, OSO2C6H4NO2-p; R4, R5 = H, (un)substituted alkyl, alkoxy, (hetero)cycloalkyl, (hetero)aryl; or R5 = N(R4)2; R6 = COR7 or CO2R7; R7 = alkyl; Y = sidechains containing specified benzene, indene, benzofuran, indole, benzimidazole, and analogous aromatic nuclei]. For example, 2-chloro-5-cyanopyridine was reduced with Dibal-H to give the 5-aldehyde, which was methylenated with Ph3P+MeBr- and KOBu-tert to give 2-chloro-5-vinylpyridine. The vinyl compound was dihydroxylated with AD-mix-β® to give the (R)-diol, which was O-tosylated with p-MeC6H4SO2Cl and then silylated with tert-BuSiMe2Cl to give the intermediate III. Coupling of III with 4-nitrophenethylamine, protection with di-tert-Bu dicarbonate, and reduction of the nitro group with concomitant dechlorination gave the final, silylated intermediate IV.

IT 173901-05-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; processes for preparing substituted pyridines useful as intermediates for β-adrenergic receptor agonists)

RN 173901-05-8 HCAPLUS

CN Carbamic acid, [2-(4-aminophenyl)ethyl][(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



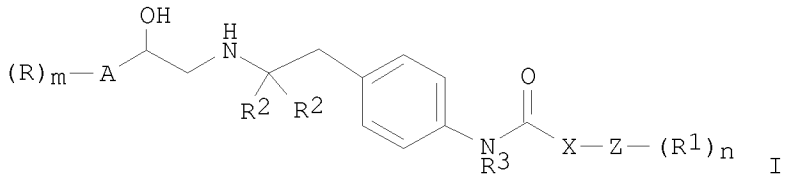
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:716519 HCAPLUS
DOCUMENT NUMBER: 135:242138
TITLE: Preparation of amide derivatives as β3 adrenergic receptor agonists
INVENTOR(S): Ashton, Wallace T.; Mathvink, Robert; Naylor, Elizabeth M.; Parmee, Emma R.; Weber, Ann E.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: Brit. UK Pat. Appl., 45 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

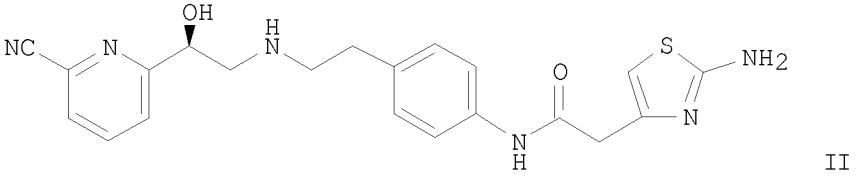
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
GB 2356197	A	20010516	GB 2000-24805		20001010 <--
US 6291491	B1	20010918	US 2000-689169		20001012 <--
PRIORITY APPLN. INFO.:			US 1999-158871P	P	19991012

GI

Updated Search



I



II

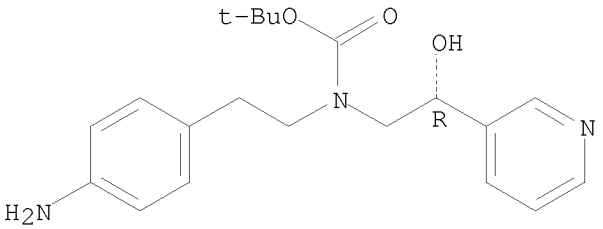
AB Pyridine amide derivs. I (m = 0-5; n = 0-5; A = benzene, 5- or 6-membered heterocyclic ring with 1-4 atoms = O, S, N or benzene fused to a heterocyclic ring; X = C1-C3 alkylene, O, amino, bond; Z = Ph, naphthyl, 5- or 6-membered heterocyclic ring, carbocyclic fused benzene, benzene fused to a heterocyclic ring; R, R1 = (un)-substituted C1-10-alkyl, C3-8-cycloalkyl, oxo, halo, CN, etc.; R2 = R3 H, C1-10-alkyl) were prepared for use as β3 adrenergic receptor agonists (no data). Thus II was prepared in 47% yield in a multistep synthesis for use in the treatment of diabetes, obesity, lowering of triglyceride and cholesterol levels or for raising high d. lipoprotein levels or to decrease gut motility and to reduce airway neurogenic inflammation.

IT 173901-05-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amide derivs. as β3 adrenergic receptor agonists)

RN 173901-05-8 HCAPLUS

CN Carbamic acid, [2-(4-aminophenyl)ethyl][(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 11 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:716518 HCAPLUS

DOCUMENT NUMBER: 135:226885

TITLE: Preparation of guanidine and ethylenediamine derivatives as selective β3 adrenergic receptor agonists

INVENTOR(S): Brockunier, Linda; Parmee, Emma R.; Weber, Ann E.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

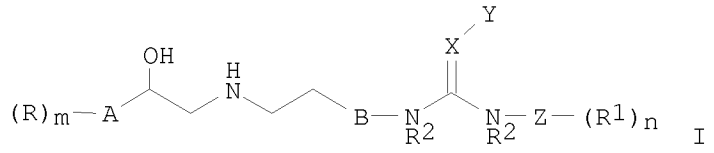
SOURCE: Brit. UK Pat. Appl., 46 pp.

Updated Search

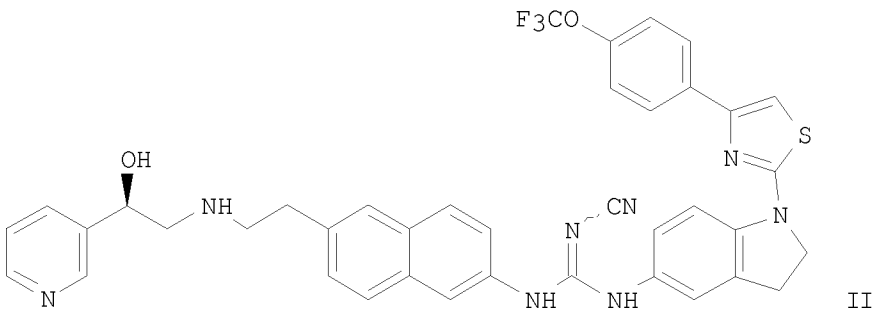
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2356196	A	20010516	GB 2000-24063	20001002 <--

PRIORITY APPLN. INFO.: US 1999-157576P P 19991004
GI



I



II

AB The pyridine guanidine and ethylenediamine derivs. I (m = 0-5; n = 0-5; A = benzene, 5- or 6-membered (fused)heterocycle with 1-4 atoms = O, S, N; B = Ph, naphthyl, (fused)heterocycle, benzene fused to a C5-C10 carbocyclic ring or to heterocyclic ring; X = CH, N; Y = NO2, CN, SO2 group; Z = B, or C1-C10 (un)substituted alkyl; R = OH, halo, CN, etc. substituted C1-C10 alkyl; R1 = R or B optionally substituted; R2 = H, Me or two R2 groups together form a 5- or 6-membered ring) were prepared for use as β3 adrenergic receptor agonists (no data). Thus II was prepared in a multistep synthesis for use in the treatment of diabetes, obesity, lowering of triglyceride and cholesterol levels or for raising high d. lipoprotein levels or to reduce airway neurogenic inflammation.

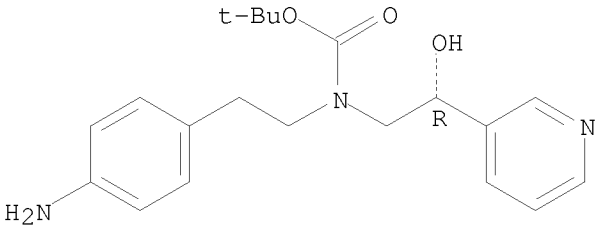
IT 173901-05-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of guanidine and ethylenediamine derivs. as selective β3 adrenergic receptor agonists)

RN 173901-05-8 HCAPLUS

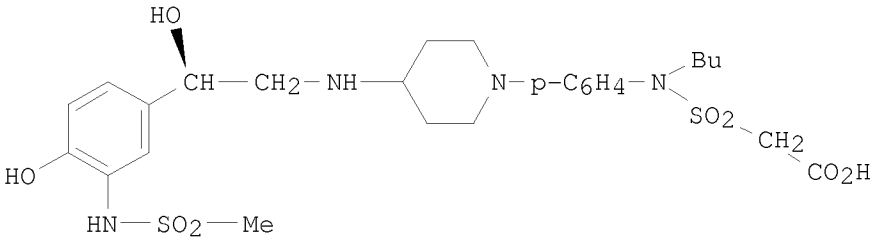
CN Carbamic acid, [2-(4-aminophenyl)ethyl][(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Updated Search



L9 ANSWER 12 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:591187 HCAPLUS
DOCUMENT NUMBER: 135:352336
TITLE: Novel (4-Piperidin-1-yl)-phenyl Sulfonamides as Potent and Selective Human β3 Agonists
AUTHOR(S): Hu, B.; Ellingboe, J.; Han, S.; Largis, E.; Lim, K.; Malamas, M.; Mulvey, R.; Niu, C.; Oliphant, A.; Pelletier, J.; Singanallore, T.; Sum, F.-W.; Tillett, J.; Wong, V.
CORPORATE SOURCE: Chemical Sciences, Wyeth-Ayerst Research, Pearl River, NY, 10965, USA
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(8), 2045-2059
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:352336
GI



I

AB A series of novel (4-piperidin-1-yl)-Ph sulfonamides was prepared and evaluated for their biol. activity on the human β3-adrenergic receptor (AR). Replacement of the 3,4-dihydroxyl group of the catechol moiety with 4-hydroxyl-3-Me sulfonamide on the left-hand side of the compds. resulted in a number of potent full agonists at the β3 receptor. Modification of the right-hand side of the compds. by incorporation of a free carboxylic acid resulted in a few potent human β3 agonists with low affinities for β1- and β2-ARs. N-Alkyl substitution on the 4-piperidin-1-yl-phenylamine further increased the β3 potency while maintaining the selectivity. For example, sulfonamide I is a potent full β3 agonist (EC50=0.004 μM, IA=1.0) with >500-fold selectivity over β1- and β2-ARs.
IT 173901-95-6P, L 770644

Updated Search

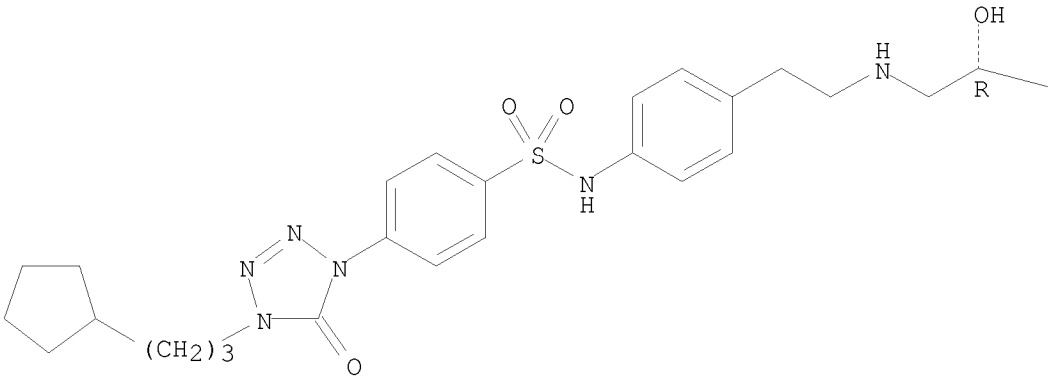
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation and β-agonist activity of piperidinyl Ph sulfonamides)

RN 173901-95-6 HCAPLUS

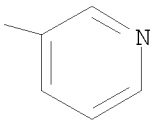
CN Benzenesulfonamide, 4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:563171 HCAPLUS

DOCUMENT NUMBER: 136:31230

TITLE: Determination of a β3-agonist in human plasma by LC/MS/MS with semi-automated 48-well diatomaceous earth plate

AUTHOR(S): Wang, A. Q.; Fisher, A. L.; Hsieh, J.; Cairns, A. M.; Rogers, J. D.; Musson, D. G.

CORPORATE SOURCE: Merck Research Laboratories, Merck & Co., Inc., West Point, PA, 19486, USA

SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2001), 26(3), 357-365
CODEN: JPBADA; ISSN: 0731-7085

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

Updated Search

LANGUAGE: English

AB Methods for the determination of a β3-agonist (A) in human plasma were developed and compared based on HPLC with tandem mass spectrometric (MS/MS) detection using a turbo ion spray (TIS) interface. Drug and internal standard were isolated from plasma by three sample preparation methods, liquid-liquid extraction, Chem Elut cartridges and 48-well diatomaceous earth plates, that successively improved sample throughput for LC/MS/MS. MS/MS detection was performed on a PE Sciex API 365 tandem mass spectrometer operated in pos. ion mode and using multiple reaction monitoring (MRM). The precursor/product ion combinations of m/z 625/607 and 653/515 were used to quantify A and internal standard, resp., after chromatog. separation of the analytes. Using liquid-liquid extraction and Chem Elut cartridges, the assay concentration range was 0.5-100 ng/mL. Using diatomaceous earth plates, the concentration range of the assay was extended to 0.5-200 ng/mL. For all three assays, the statistics for precision and accuracy is comparable. The assay accuracy ranged from 91-107% and intraday precision as measured by the coefficient of variation (CV) ranged 2-10%. The sample throughput was tripled when the diatomaceous earth plate method was compared with the original liquid-liquid extraction method.

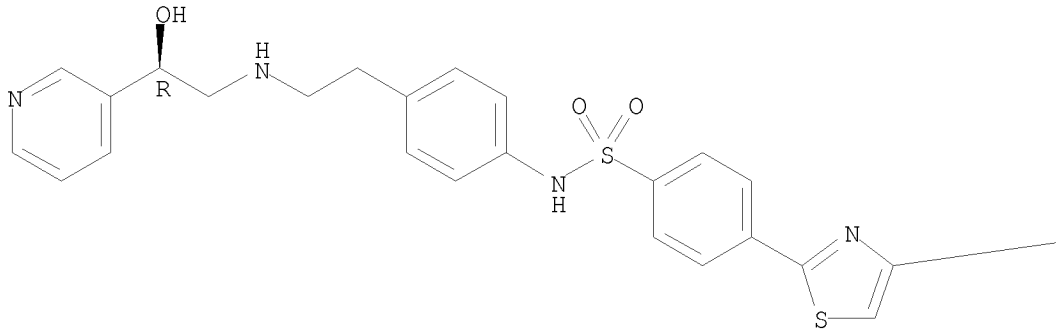
IT 211031-01-5
RL: ANT (Analyte); ANST (Analytical study)
(determination of a β3-agonist in human plasma by LC/MS/MS with semi-automated 48-well diatomaceous earth plate)

RN 211031-01-5 HCAPLUS

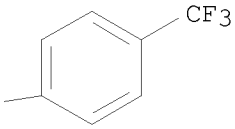
CN Benzenesulfonamide, N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[4-[4-(trifluoromethyl)phenyl]-2-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



Updated Search



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:240842 HCAPLUS
DOCUMENT NUMBER: 135:71234
TITLE: β3-Adrenoceptor agonist-induced increases in lipolysis, metabolic rate, facial flushing, and reflex tachycardia in anesthetized rhesus monkeys
AUTHOR(S): Hom, Gary J.; Forrest, Michael J.; Bach, Thomas J.; Brady, Edward; Candelore, Mari Rios; Cascieri, Margaret A.; Fletcher, Donna J.; Fisher, Michael H.; Iliff, Susan A.; Mathvink, Robert; Metzger, Joseph; Pecore, Victor; Saperstein, Richard; Shih, Thomas; Weber, Ann E.; Wyvratt, Matthew; Zafian, Peter; Macintyre, D. Euan
CORPORATE SOURCE: Department of Animal Pharmacology, Merck Research Laboratories, Rahway, NJ, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 297(1), 299-307
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of two β3-adrenergic receptor agonists, (R)-4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]benzenesulfonamide and (R)-N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)-ethyl]amino]ethyl]phenyl]-1-(4-octylthiazol-2-yl)-5-indolinesulfonamide, on indexes of metabolic and cardiovascular function were studied in anesthetized rhesus monkeys. Both compds. are potent and specific agonists at human and rhesus β3-adrenergic receptors. I.v. administration of either compound produced dose-dependent lipolysis, increase in metabolic rate, peripheral vasodilatation, and tachycardia with no effects on mean arterial pressure. The increase in heart rate in response to either compound was biphasic with an initial rapid component coincident with the evoked peripheral vasodilatation and a second more slowly developing phase contemporaneous with the evoked increase in metabolic rate. Because both compds. exhibited weak binding to and activation of rhesus β1-adrenergic receptors in vitro, it was hypothesized that the increase in heart rate may be reflexogenic in origin and proximally mediated via release of endogenous norepinephrine acting at cardiac β1-adrenergic receptors. This hypothesis was confirmed by determining that β3-adrenergic receptor agonist-evoked tachycardia was attenuated in the presence of propranolol

and in ganglion-blocked animals, under which conditions there was no reduction in the evoked vasodilatation, lipolysis, or increase in metabolic rate. It is not certain whether the β3-adrenergic receptor-evoked vasodilatation is a direct effect of compds. at β3-adrenergic receptors in the peripheral vasculature or is secondary to the release or generation of an endogenous vasodilator. Peripheral vasodilatation in response to β3-adrenergic receptor agonist administration was not attenuated in animals administered mepyramine, indomethacin, or calcitonin gene-related peptide8-37. These findings are consistent with a direct vasodilator effect of β3-adrenergic receptor agonists.

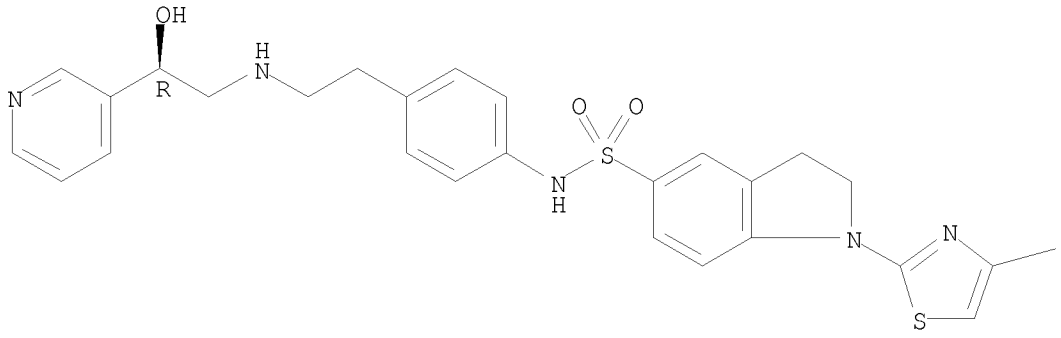
IT 173901-90-1
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β3-adrenoceptor agonist-induced increases in lipolysis, metabolic rate, facial flushing, and reflex tachycardia in anesthetized rhesus monkeys)

RN 173901-90-1 HCAPLUS

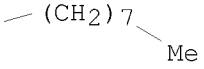
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-1-(4-octyl-2-thiazolyl)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

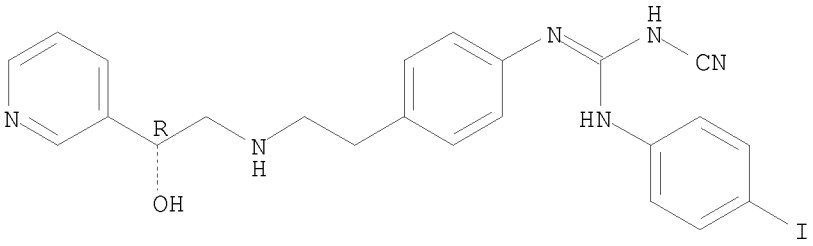


REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Updated Search

L9 ANSWER 15 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:118625 HCAPLUS
DOCUMENT NUMBER: 134:304966
TITLE: Human β3 adrenergic receptor agonists containing cyanoguanidine and nitroethylenediamine moieties
AUTHOR(S): Brockunier, L. L.; Candelore, M. R.; Cascieri, M. A.; Liu, Y.; Tota, L.; Wyvratt, M. J.; Fisher, M. H.; Weber, A. E.; Parmee, E. R.
CORPORATE SOURCE: Departments of Medicinal Chemistry, Biochemistry and Physiology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(3), 379-382
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pyridineethanolamine derivs. containing cyanoguanidine or nitroethylenediamine moieties were examined as human β3 adrenergic receptor (AR) agonists. Notably, indoline derivs. were potent β3 AR agonists (β3 EC50=13 and 19 nM, resp.), which showed good selectivity over binding to and minimal activation of the β1 and β2 adrenergic receptors. Pyridineethanolamine derivs. containing a cyanoguanidine or nitroethylenediamine moiety were shown to be potent, selective human β3 adrenergic receptor agonists.
IT 335383-65-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(human β3 adrenergic receptor agonists containing cyanoguanidine and nitroethylenediamine moieties)
RN 335383-65-8 HCAPLUS
CN Guanidine, N-cyano-N'-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-N''-(4-iodophenyl)- (CA INDEX NAME)

Absolute stereochemistry.

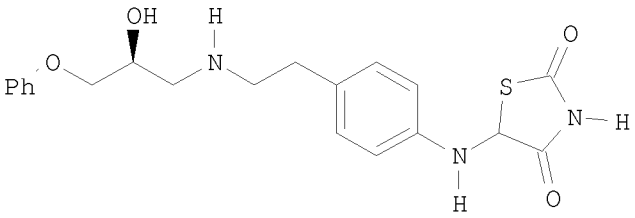


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:816874 HCAPLUS
DOCUMENT NUMBER: 134:110104
TITLE: Potent, selective aminothiazolidinediones agonists of the human β3 adrenergic receptor
AUTHOR(S): Malamas, Michael S.; Largis, Elwood; Gunawan, Iwan;

Updated Search

Li, Zenan; Tillett, Jeffrey; Han, Stella Ching-Hsien; Mulvey, Ruth
CORPORATE SOURCE: Wyeth-Ayerst Research, Inc., Princeton, NJ, 08543-8000, USA
SOURCE: Medicinal Chemistry Research (2000), 10(3), 164-177
CODEN: MCREEB; ISSN: 1054-2523
PUBLISHER: Birkhaeuser Boston
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

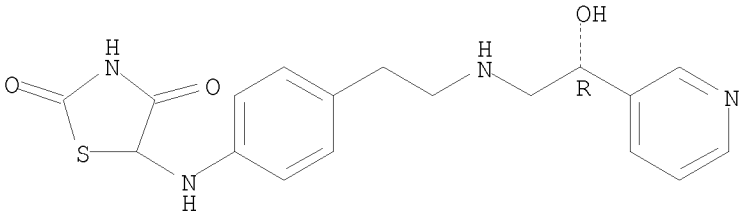


I

AB A cloned human β3 adrenergic receptor assay was used to identify potent and selective β3 agonists. The thiazolidinedione moiety has been identified as a new pharmacophore for the human β3 adrenergic receptor. The versatility of the thiazolidinedione pharmacophore was demonstrated in both the arylethanolamine and phenylpropanolamine families of β3 agonists, where potent and selective compds. have been synthesized. Thiazolidinedione I, a potent and selective human β3 agonist, increased thermogenesis and lowered plasma glucose levels in the db/db mice.

IT 321575-14-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminothiazolidinediones as agonists of human β3 adrenergic receptor)
RN 321575-14-8 HCAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]amino]- (CA INDEX NAME)

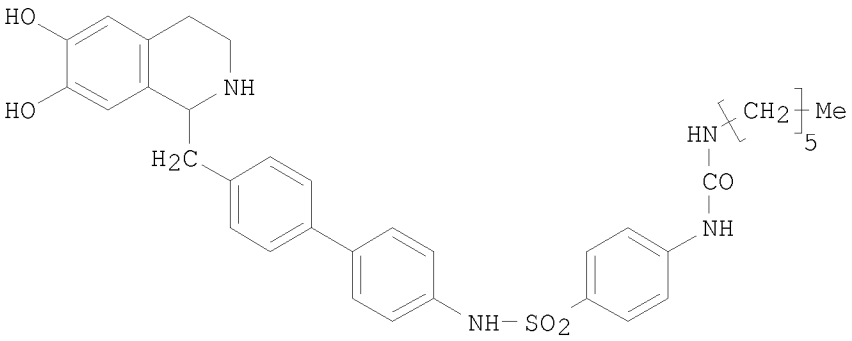
Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Updated Search

L9 ANSWER 17 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:719697 HCAPLUS
DOCUMENT NUMBER: 134:50979
TITLE: Tetrahydroisoquinoline derivatives containing a benzenesulfonamide moiety as potent, selective human β3 adrenergic receptor agonists
AUTHOR(S): Parmee, E. R.; Brockunier, L. L.; He, J.; Singh, S. B.; Candelore, M. R.; Cascieri, M. A.; Deng, L.; Liu, Y.; Tota, L.; Wyvratt, M. J.; Fisher, M. H.; Weber, A. E.
CORPORATE SOURCE: Departments of Medicinal Chemistry, Molecular Systems, and Biochemistry and Molecular Pharmacology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(20), 2283-2286
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Tetrahydroisoquinoline derivs. containing a 4-(hexylureido)benzenesulfonamide were examined as human β3 adrenergic receptor (AR) agonists. Notably, 4,4-biphenyl derivative I was a 6 nM full agonist of the β3 AR. A naphthyloxy compound (β3 EC50=78 nM) did not activate the β1 and β2 ARs at 10 μM, and showed >1000-fold selectivity over binding to the β1 and β2 ARs.

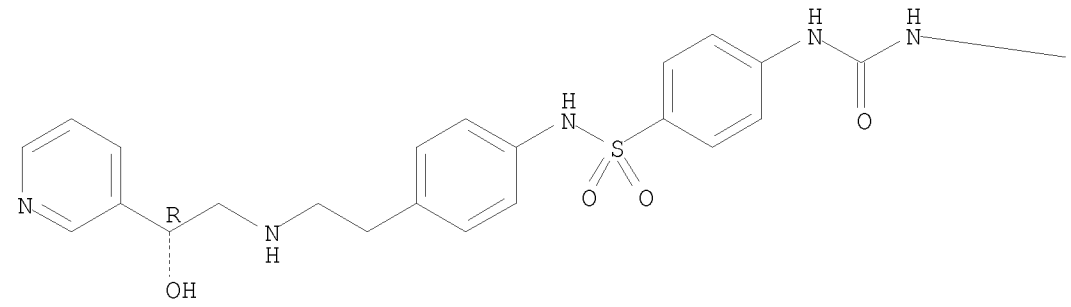
IT 173901-42-3
RL: PRP (Properties)
(preparation of tetrahydroisoquinoline benzenesulfonamides as β3 adrenergic receptor agonists)

RN 173901-42-3 HCAPLUS
CN Benzenesulfonamide, 4-[[(hexylamino)carbonyl]amino]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

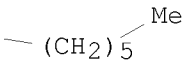
Absolute stereochemistry.

Updated Search

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:683152 HCAPLUS
DOCUMENT NUMBER: 134:437
TITLE: Discovery of a Potent, Orally Bioavailable β3 Adrenergic Receptor Agonist, (R)-N-[4-[2-[[2-Hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[4-[4-(trifluoromethyl)phenyl]thiazol-2-yl]benzenesulfonamide
AUTHOR(S): Mathvink, Robert J.; Tolman, J. Samuel; Chitty, Dawn; Candelore, Mari R.; Cascieri, Margaret A.; Colwell, Lawrence F., Jr.; Deng, Liping; Feeney, William P.; Forrest, Michael J.; Hom, Gary J.; MacIntyre, D. Euan; Miller, Randall R.; Stearns, Ralph A.; Tota, Laurie; Wyvratt, Matthew J.; Fisher, Michael H.; Weber, Ann E.
CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(21), 3832-3836
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:437

AB As part of the authors investigation into the development of orally bioavailable β3 adrenergic receptor agonists, the authors have identified a series of pyridylethanolamine analogs possessing a substituted thiazole benzenesulfonamide pharmacophore that are potent human β3 agonists with excellent selectivity against other human β receptor subtypes. Several of these compds. also exhibited an improved pharmacokinetic profile in dogs. For example, the title compound is a potent full β3 agonist (EC50 = 3.6 nM, 94% activation) with >600-fold selectivity over the human β1 and β2 receptors, which also displays good oral bioavailability in several mammalian species, as well as an extended duration of action in inducing hyperglycerolemia. The

use of such agents to treat obesity is discussed.

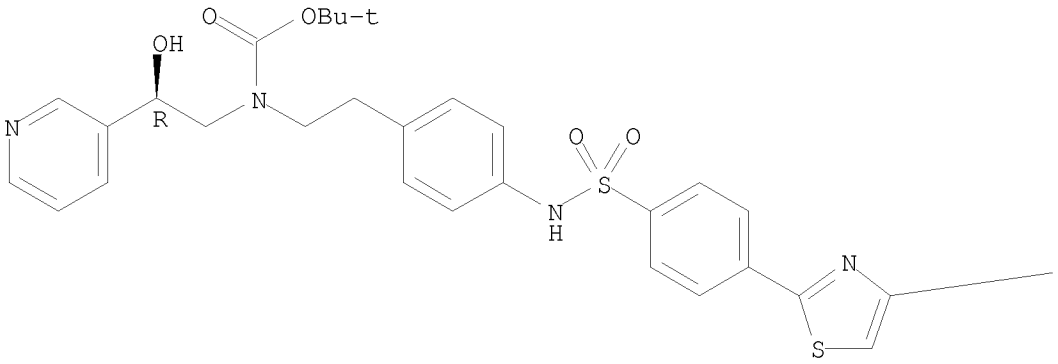
IT 308368-70-9P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(discovery of a potent and orally bioavailable β3 adrenergic receptor agonist fluoromethylphenylthiazolylbenzenesulfonamide derivative in relation to pharmacokinetics and induction of hyperglycerolemia and treatment of obesity)

RN 308368-70-9 HCAPLUS

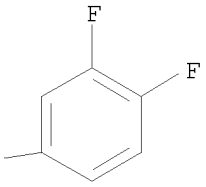
CN Carbamic acid, [2-[4-[[[4-[4-(3,4-difluorophenyl)-2-thiazolyl]phenyl]sulfonyl]amino]phenyl]ethyl][(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

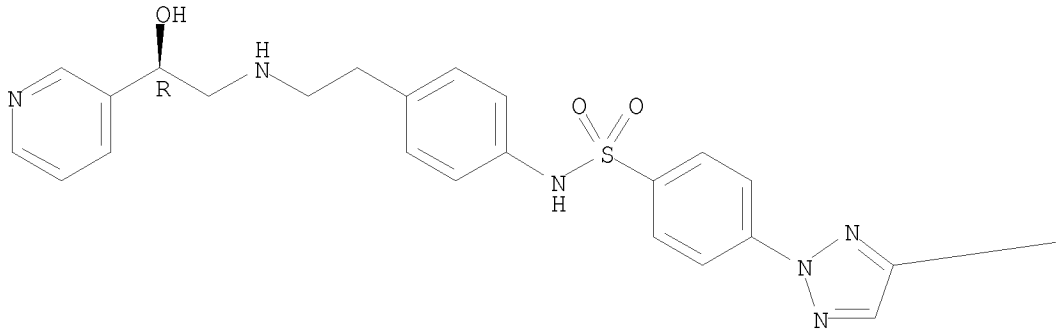
L9 ANSWER 19 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:619253 HCAPLUS
DOCUMENT NUMBER: 133:362736
TITLE: Human β3-adrenergic receptor agonists containing 1,2,3-triazole-substituted benzenesulfonamides

Updated Search

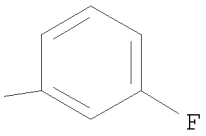
AUTHOR(S): Brockunier, L. L.; Parmee, E. R.; Ok, H. O.; Candelore, M. R.; Cascieri, M. A.; Colwell, L. F.; Deng, L.; Feeney, W. P.; Forrest, M. J.; Hom, G. J.; MacIntyre, D. E.; Tota, L.; Wyvratt, M. J.; Fisher, M. H.; Weber, A. E.
CORPORATE SOURCE: Departments of Medicinal Chemistry, Biochemistry and Physiology, Pharmacology, and Comparative Medicine, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(18), 2111-2114
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Compds. containing a 1,2,3-triazole-substituted benzenesulfonamide were prepared (data not shown) and found to be potent and selective human β3-adrenergic receptor agonists. The most interesting compound, a trifluoromethylbenzyl analog (β3 EC50=3.1 nM with 1500-fold selectivity over binding to both β1- and β2 receptors), stimulates lipolysis in the rhesus monkey (ED50=0.36 mg/kg) and is 25% orally bioavailable in the dog.
IT 307529-22-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
((triazolyl)benzenesulfonamides and their activity as β3-adrenergic receptor agonists)
RN 307529-22-2 HCAPLUS
CN Benzenesulfonamide, 4-[4-(3-fluorophenyl)-2H-1,2,3-triazol-2-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

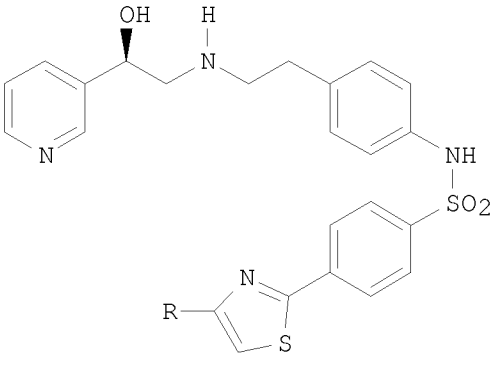


Updated Search



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:595506 HCAPLUS
DOCUMENT NUMBER: 133:335183
TITLE: Potent, selective 3-pyridylethanolamine β3 adrenergic receptor agonists possessing a thiazole benzenesulfonamide pharmacophore
AUTHOR(S): Mathvink, R. J.; Tolman, J. S.; Chitty, D.; Candelore, M. R.; Cascieri, M. A.; Colwell, L. F.; Deng, L.; Feeney, W. P.; Forrest, M. J.; Hom, G. J.; MacIntyre, D. E.; Tota, L.; Wyvratt, M. J.; Fisher, M. H.; Weber, A. E.
CORPORATE SOURCE: Department of Medicinal Chemistry, Biochemistry and Physiology, Pharmacology, and Comparative Medicine, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(17), 1971-1973
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

Updated Search

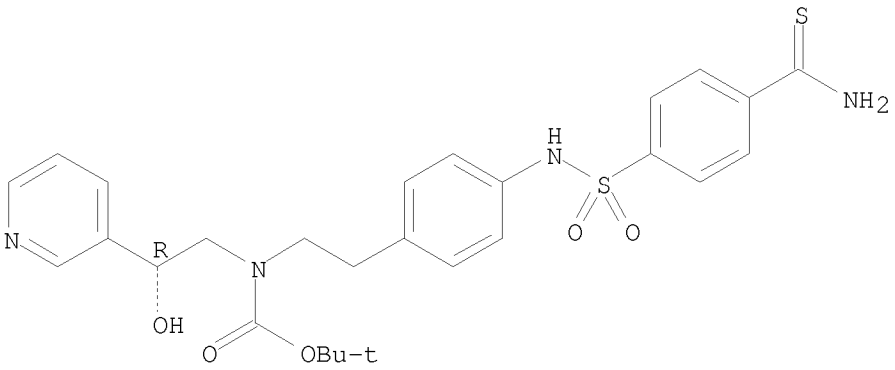
AB A series of thiazole benzenesulfonamide-substituted 3-pyridylethanolamines, e.g. I (R = octyl, hexyl, etc.), were prepared and evaluated for their human β3 adrenergic receptor agonist activity. Incorporation of aryl and heteroaryl substitution in the 4-position of the thiazole ring resulted in a number of highly potent and selective β3 agonists. Results of preliminary in vivo evaluation of several of these compds. is described.

IT 211031-93-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization with chloroketones)

RN 211031-93-5 HCAPLUS

CN Carbamic acid, [2-[4-[[[4-(aminothioxomethyl)phenyl]sulfonyl]amino]phenyl]ethyl][(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:496101 HCAPLUS

DOCUMENT NUMBER: 133:232362

TITLE: Substituted oxazole benzenesulfonamides as potent human β3 adrenergic receptor agonists

AUTHOR(S): Ok, H. O.; Reigle, L. B.; Candelore, M. R.; Cascieri, M. A.; Colwell, L. F.; Deng, L.; Feeney, W. P.; Forrest, M. J.; Hom, G. J.; MacIntyre, D. E.; Strader, C. D.; Tota, L.; Wang, P.; Wyvratt, M. J.; Fisher, M. H.; Weber, A. E.

CORPORATE SOURCE: Departments of Medicinal Chemistry, Biochemistry and Physiology, Pharmacology, and Comparative Medicine, Merck Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(14), 1531-1534
CODEN: BMCLE8; ISSN: 0960-894X

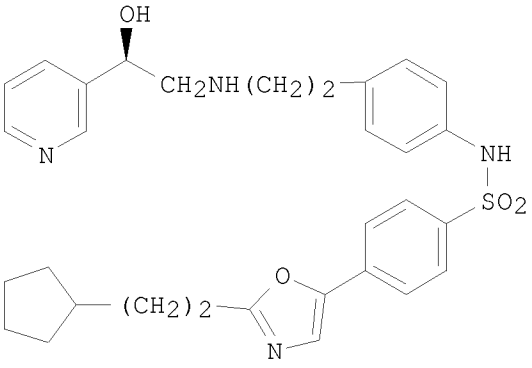
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

Updated Search



I

AB As a part of our investigation into the development of orally bioavailable β3 adrenergic receptor agonists, we have identified a series of substituted oxazole derivs. that are potent β3 agonists with excellent selectivity against other β receptors. Several of these compds. showed excellent oral bioavailability in dogs. The cyclopentylethyloxazole (I) is a potent β3 agonist (EC50=14 nM, 84% activation) with 340-fold and 160-fold selectivity over β1 and β2 receptors, resp., and has 38% oral bioavailability in dogs.

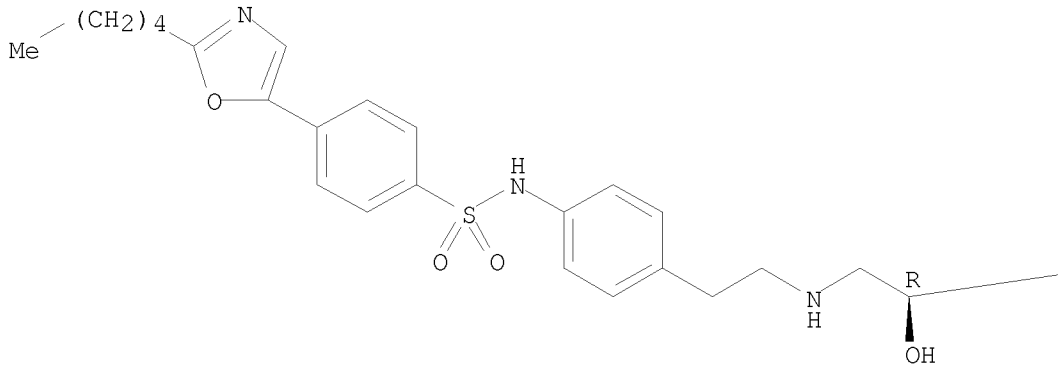
IT 173902-02-8P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(preparation and structure-activity relations of substituted oxazole benzenesulfonamides as potent human β3 adrenergic receptor agonists)

RN 173902-02-8 HCAPLUS

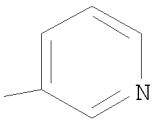
CN Benzenesulfonamide, N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(2-pentyl-5-oxazolyl)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

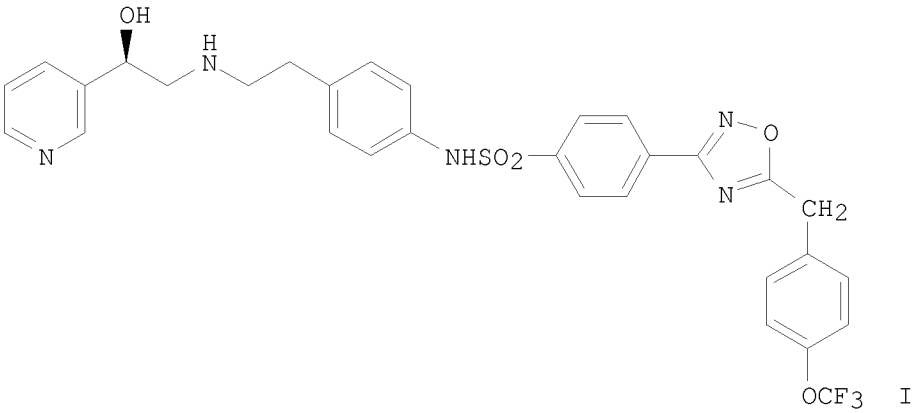


Updated Search



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 22 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:458487 HCAPLUS
DOCUMENT NUMBER: 133:252372
TITLE: Synthesis and SAR of benzyl and phenoxymethylene oxadiazole benzenesulfonamides as selective β3 adrenergic receptor agonist antiobesity agents
AUTHOR(S): Biftu, Tesfaye; Feng, Dennis D.; Liang, Gui-Bai; Kuo, Howard; Qian, Xiaoxia; Naylor, Elizabeth M.; Colandrea, Vincent J.; Candelore, Mari R.; Cascieri, Margaret A.; Colwell, Lawrence F., Jr.; Forrest, Michael J.; Hom, Gary J.; MacIntyre, D. Euan; Stearns, Ralph A.; Strader, Catherine D.; Wyvratt, Matthew J.; Fisher, Michael H.; Weber, Ann E.
CORPORATE SOURCE: Departments of Medicinal Chemistry, Biochemistry & Physiology, Drug Metabolism, Pharmacology and Comparative Medicine, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(13), 1431-1434
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

Updated Search

AB Benzyl and phenoxymethylene substituted oxadiazoles were prepared and are potent and orally bioavailable β3 adrenergic receptor (AR) agonists. The 4-trifluormethoxybenzyloxadiazole I has an EC50 of 8 nM in the β3 AR agonist assay with 100-fold selectivity over β1 and β2 AR binding inhibition activity. Its oral bioavailability in dogs is 30 ± 4%, with a half-life of 3.8 ± 0.4 h. In the anesthetized rhesus, I evoked a dose-dependent glycerolemia (ED50Gly = 0.15 mg/kg). Under these conditions a heart rate increase of 15% was observed at a dose level of 10 mg/kg.

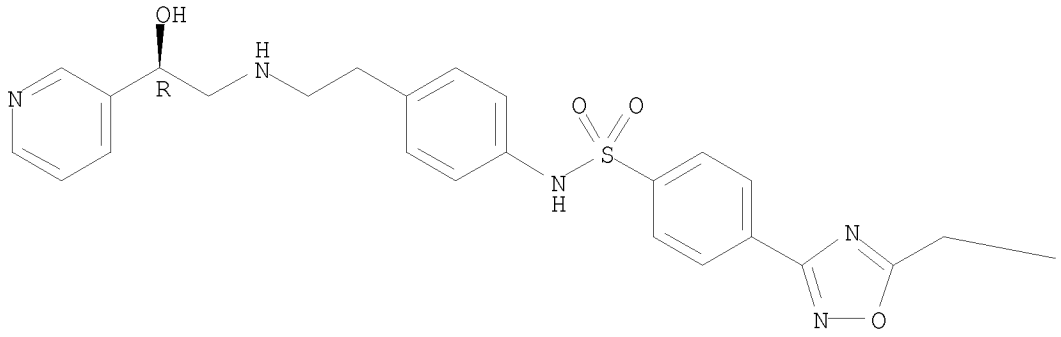
IT 200499-07-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of oxadiazolylbenzenesulfonamides as β3 adrenergic agonists and antiobesity agents)

RN 200499-07-6 HCAPLUS

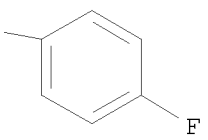
CN Benzenesulfonamide, 4-[5-[(4-fluorophenyl)methyl]-1,2,4-oxadiazol-3-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

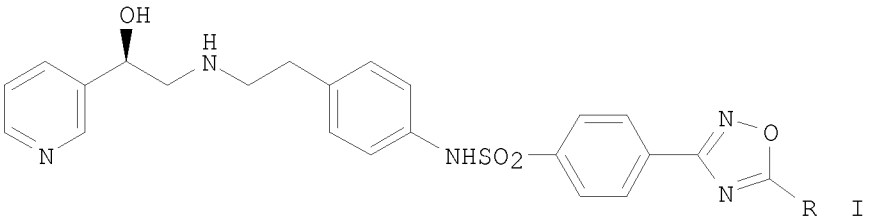


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

Updated Search

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:458486 HCAPLUS
DOCUMENT NUMBER: 133:252371
TITLE: Discovery of an orally bioavailable alkyl oxadiazole β3 adrenergic receptor agonist
AUTHOR(S): Feng, Danqing D.; Biftu, Tesfaye; Candelore, Mari R.; Cascieri, Margaret A.; Colwell, Lawrence F., Jr.; Deng, Liping; Feeney, William P.; Forrest, Michael J.; Hom, Gary J.; MacIntyre, D. Euan; Miller, Randall R.; Stearns, Ralph A.; Strader, Catherine D.; Tota, Laurie; Wyvratt, Matthew J.; Fisher, Michael H.; Weber, Ann E.
CORPORATE SOURCE: Departments of Medicinal Chemistry, Biochemistry & Physiology, Drug Metabolism, Pharmacology and Comparative Medicine, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(13), 1427-1429
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



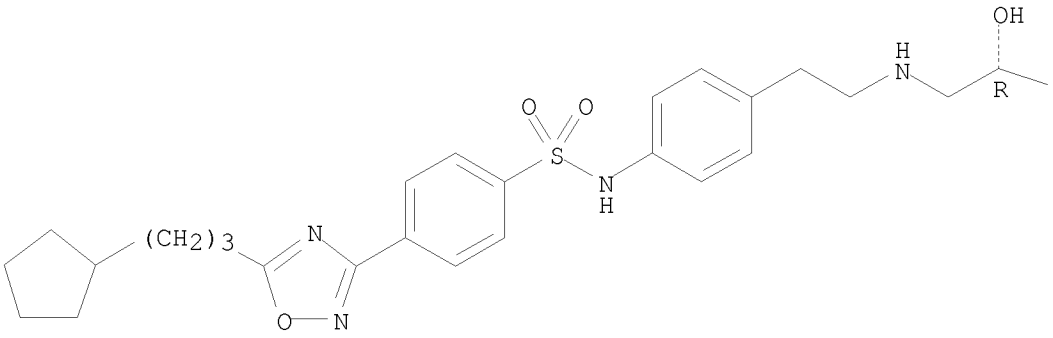
AB The oxadiazole derivs. I [R = (un)substituted alkyl] were prepared by treating the aniline fragment with 4-NCC6H4SO2Cl and NH2OH, followed by cyclization with RCO2H or RCOCl and deprotection. I [R = pentyl] is a potent and selective β3 adrenergic receptor agonist (β3 EC50 = 23 nM, β1 IC50 = 3000 nM, β2 IC50 = 3000 nM). The compound has high oral bioavailability in dogs (62%) and rats (36%) and is among the most orally bioavailable β3 adrenergic receptor agonists reported to date.

IT 173901-47-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of oxadiazolylbenzenesulfonamides as selective β3 adrenergic receptor agonists)
RN 173901-47-8 HCAPLUS
CN Benzenesulfonamide, 4-[5-(3-cyclopentylpropyl)-1,2,4-oxadiazol-3-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

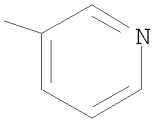
Absolute stereochemistry.

Updated Search

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 24 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:259977 HCAPLUS
DOCUMENT NUMBER: 132:274338
TITLE: Use of beta-3-agonist compounds for inhibition of uterine contractions
INVENTOR(S): Advenier, Charles; Manara, Luciano
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021508	A2	20000420	WO 1999-FR2308	19990929 <--
WO 2000021508	A3	20001026		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2784582	A1	20000421	FR 1998-12877	19981014 <--
FR 2784582	B3	20001124		

Updated Search

AU 9958686	A	20000501	AU 1999-58686		19990929	<--
EP 1121108	A2	20010808	EP 1999-946255		19990929	<--
EP 1121108	B1	20030402				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO						
JP 2002527377	T	20020827	JP 2000-575484		19990929	
AT 235899	T	20030415	AT 1999-946255		19990929	
PT 1121108	T	20030829	PT 1999-946255		19990929	
ES 2195612	T3	20031201	ES 1999-946255		19990929	
US 6310050	B1	20011030	US 2001-807342		20010524	<--
PRIORITY APPLN. INFO.:			FR 1998-12877	A	19981014	
			WO 1999-FR2308	W	19990929	

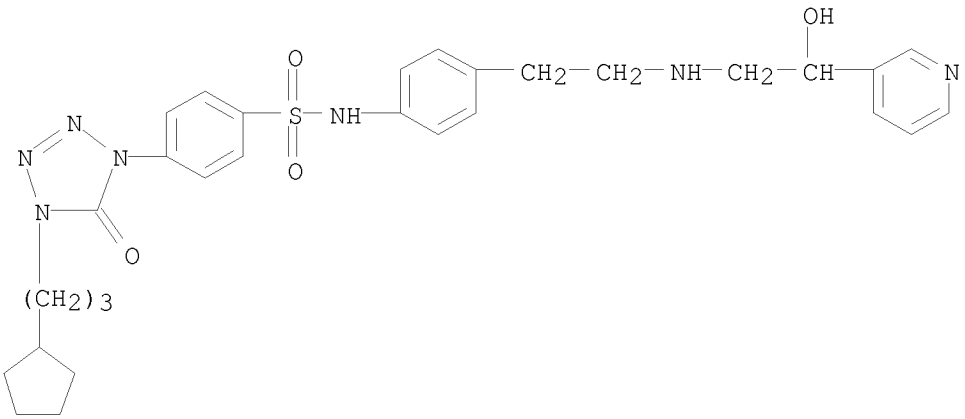
OTHER SOURCE(S): MARPAT 132:274338

AB The invention concerns the use of a compound with β3-agonist activity for preparing a medicine designed to inhibit uterine contractions, to be used as tocolytic or for treating and/or preventing dysmenorrhea (Markush structure given). The contraction inhibitory effect of 10-8-3x10-5 M concentration of a tetrahydronaphtalyl chlorophenyl ethanamine was equal with salbutamol on the human myometrium.

IT 173900-99-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of beta-3-agonist compds. for inhibition of uterine contractions)

RN 173900-99-7 HCAPLUS

CN Benzenesulfonamide, 4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 25 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:175676 HCAPLUS
DOCUMENT NUMBER: 132:222456
TITLE: Preparation of 4-quinolinemethanol derivatives as purine receptor antagonists. (II)
INVENTOR(S): Gillespie, Roger John; Lerpiniere, Joanne; Giles, Paul Richard; Adams, David Reginald; Knutsen, Lars Jacob Stray; Cliffe, Ian Anthony

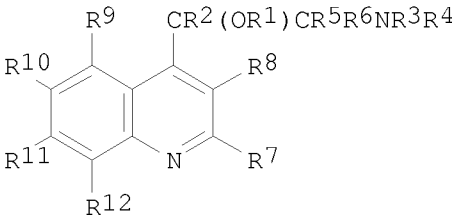
Updated Search

PATENT ASSIGNEE(S): Cerebrus Pharmaceuticals Limited, UK
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000013682	A2	20000316	WO 1999-GB2924	19990903 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9956402	A	20000327	AU 1999-56402	19990903 <--
EP 1107761	A2	20010620	EP 1999-943124	19990903 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6608085	B1	20030819	US 2001-786472	20010509

PRIORITY APPLN. INFO.:		GB 1998-19384 A	19980904
		WO 1999-GB2924 W	19990903

OTHER SOURCE(S): MARPAT 132:222456
GI



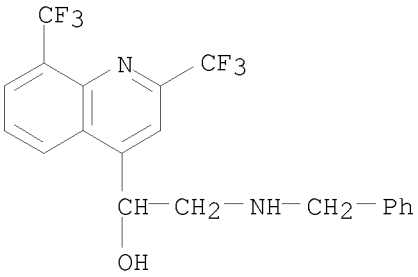
I

AB The title compds. I [R1 = H, alkyl; R2 = H, alkyl, aryl, heterocyclic rings; R3, R4 = H, alkyl, aryl, COR13, CO2R13, CONR13R14, CONR13NR14R15, SO2R13, SO2NR13R14, SO2NR13NR14R15 or may form a ring; R1R4, R2R3 may form a heterocyclic ring; R5, R6 = H, alkyl, aryl, heterocyclic ring; R7-R12 = H, alkyl aryl, heterocyclic ring, OH, halo, etc.], for the treatment or prevention of a disorder in which the blocking of purine receptors, particularly adenosine receptors and more particularly A2A receptors, were prepared Binding affinities of I at A2A receptors were determined E.g., (11R,2'S)-α-(1-methyl-2-piperidinyl)-2,8-bis(trifluoromethyl)-4-quinolinemethanol was prepared

IT 261000-68-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of quinolinemethanol derivs. as purine receptor antagonists)
RN 261000-68-4 HCAPLUS

Updated Search

CN 4-Quinolinemethanol, α-[[(phenylmethyl)amino]methyl]-2,8-bis(trifluoromethyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

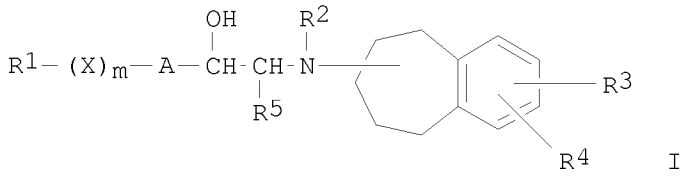
L9 ANSWER 26 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:659350 HCAPLUS
DOCUMENT NUMBER: 131:286274
TITLE: Preparation of propanolamine tetrahydro-5H-benzocycloheptene derivatives as β3 adrenergic receptor agonists
INVENTOR(S): Taniguchi, Kiyoshi; Sakurai, Minoru; Fujii, Naoaki; Hosoi, Kumi; Tomishima, Yasuyo; Takasugi, Hisashi; Sogabe, Hajime; Ishikawa, Hirofumi; Hanioka, Naomi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9951564	A1	19991014	WO 1999-JP1500	19990325 <--
W: BR, CA, CN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1070046	A1	20010124	EP 1999-909333	19990325 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002512639	T	20020423	JP 1999-544560	19990325 <--
EP 1382333	A2	20040121	EP 2003-21612	19990325
EP 1382333	A3	20040204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
US 6495546	B1	20021217	US 2000-646878	20001122
US 20020120148	A1	20020829	US 2002-74020	20020214
US 6635634	B2	20031021		

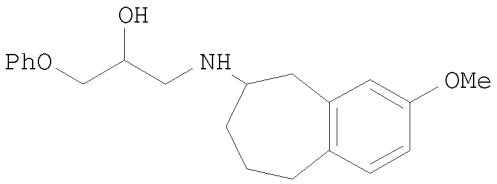
PRIORITY APPLN. INFO.:		
AU 1998-2826	A	19980406
AU 1998-5058	A	19980804
EP 1999-909333	A3	19990325
WO 1999-JP1500	W	19990325
US 2000-646878	A1	20001122

OTHER SOURCE(S): MARPAT 131:286274
GI

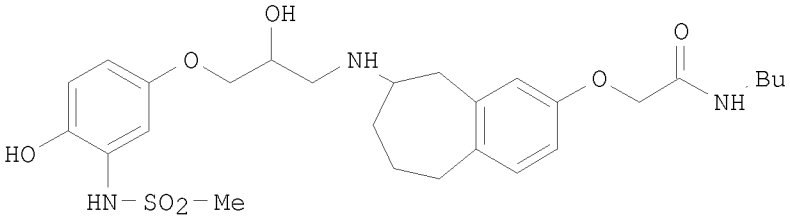
Updated Search



I



II



III

AB Propanolamine tetrahydro-5H-benzocycloheptenes (I) [where R1 = (un)substituted aryl; R2 = H or amino protective group; R3 and R4 = independently H, halogen, OH, NO2, (un)substituted NH2, carboxy, aryl, or alkyl, etc.; R5 = H, alkyl, or aryl; A = (un)substituted lower alkylene; X = O, S, SO, SO2, or NH; m = 0 or 1], and their salts, were prepared as β3 adrenergic receptor agonists. For example, (2S)-3-phenoxy-1,2-epoxypropane was couple with N-benzyl-(3-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-6-yl)amine (preparation given) and treated with Yb(III) trifluoromethanesulfonate to afford (S)-(II). Title compound (S)-(III).HCl reversed carbachol induced increase in intravesical pressure in anesthetized dogs with an ED50 (μg/kg) of 10.8. Three comparison compds. gave similar results. In a test measuring the effect of a comparison compound on cystometrogram, male rats showed an increase in bladder capacity with administration of a 0.01 mg/kg dose. In a third test, a comparison compound decreased the rhythmic contraction of the bladder to 66% of control at a dose of 0.1 mg/kg in rats. Invention compds. are useful for the treatment of pollakiuria or urinary incontinence due to their gut selective sympathomimetic, anti-ulcerous, anti-pancreatitis, lipolytic, anti-urinary incontinence and anti-pollakiuria activities.

IT 173901-95-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison compound; preparation of propanolamine tetrahydro-5H-benzocycloheptene derivs. as β3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)

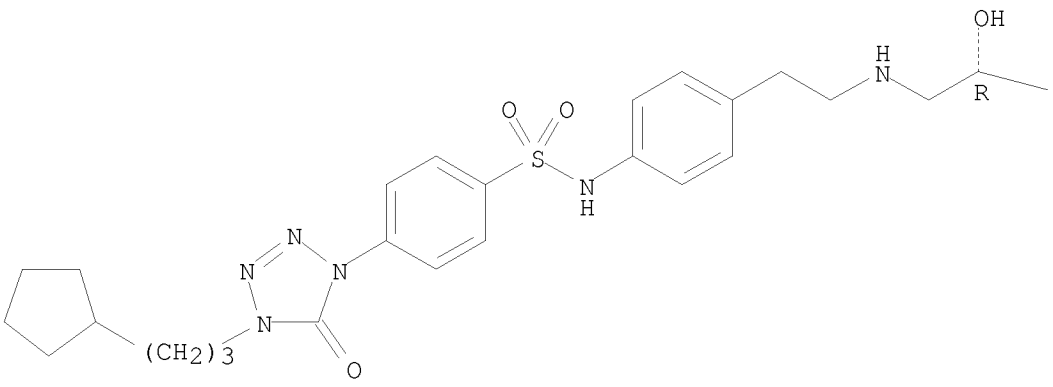
RN 173901-95-6 HCAPLUS

Updated Search

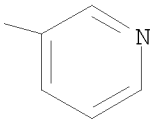
CN Benzenesulfonamide, 4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 27 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:569667 HCAPLUS
DOCUMENT NUMBER: 131:310595
TITLE: Practical chemoenzymatic synthesis of a 3-pyridylethanolamino β3 adrenergic receptor agonist
AUTHOR(S): Chung, John Y. L.; Ho, Guo-Jie; Chartrain, Michel; Roberge, Chris; Zhao, Dalian; Leazer, John; Farr, Roger; Robbins, Micheal; Emerson, Kateeta; Mathre, David J.; McNamara, James M.; Hughes, David L.; Grabowski, Edward J. J.; Reider, Paul J.
CORPORATE SOURCE: Departments of Process Research Merck Research Laboratories, Merck and Co. Inc., NJ, 07065, USA
SOURCE: Tetrahedron Letters (1999), 40(37), 6739-6743
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:310595
AB A chemoenzymic synthesis of a β3 agonist suitable for large scale

Updated Search

preparation is described. The key chiral 3-pyridylethanolamine intermediate was prepared via an improved Neber rearrangement and a yeast-mediated asym. reduction The tetrazolone fragment of the mol. was constructed via a dipolar cycloaddn. between 1-(cyclopentyl)-3-Pr azide and p-chlorosulfonyl phenylisocyanate. Sulfonamide coupling of these two intermediates under Shotten-Baumann conditions, followed by a borane reduction of the amide afforded the target compound in 20-32% overall yield from 3-acetylpyridine. The authors indicate that intermediate (E)-RC:NMeOTs (R = 3-pyridyl) showed evidence of possible low-level shock sensitivity.

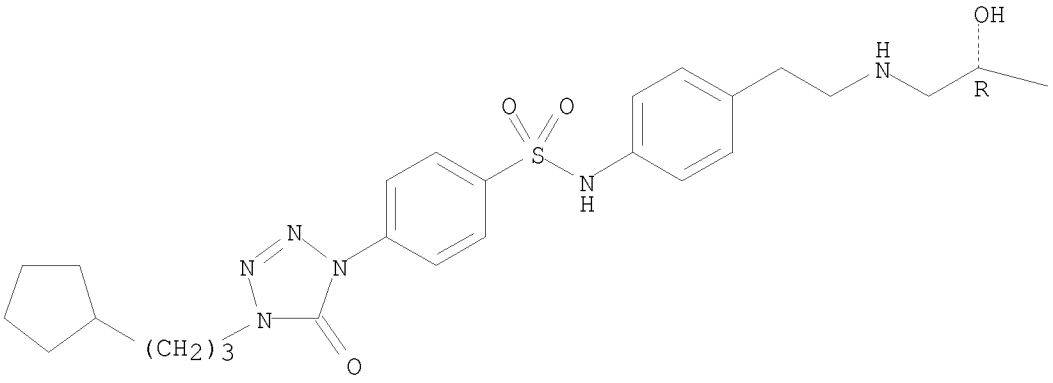
IT 173901-95-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(chemoenzymic synthesis of a pyridylethanolamino β3 adrenergic receptor agonist)

RN 173901-95-6 HCAPLUS

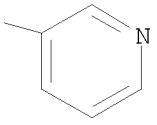
CN Benzenesulfonamide, 4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 28 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:509952 HCAPLUS
Correction of: 1999:310752
DOCUMENT NUMBER: 131:129949
Correction of: 131:73608

Updated Search

TITLE: L-770,644: a potent and selective human β3 adrenergic receptor agonist with improved oral bioavailability.

AUTHOR(S): Shih, Thomas L.; Candelore, Mari R.; Cascieri, Margaret A.; Chiu, Shuet-Hing L.; Colwell, Lawrence F., Jr.; Deng, Liping; Feeney, William P.; Forrest, Michael J.; Hom, Gary, J.; MacIntyre, D. Euan

CORPORATE SOURCE: Dep. of Med. Chem., Biochem. & Physiology, Drug Metabolism, Pharmacology and Lab. Animal Resources, Merck Research Lab., Rahway, NY, 07065, USA

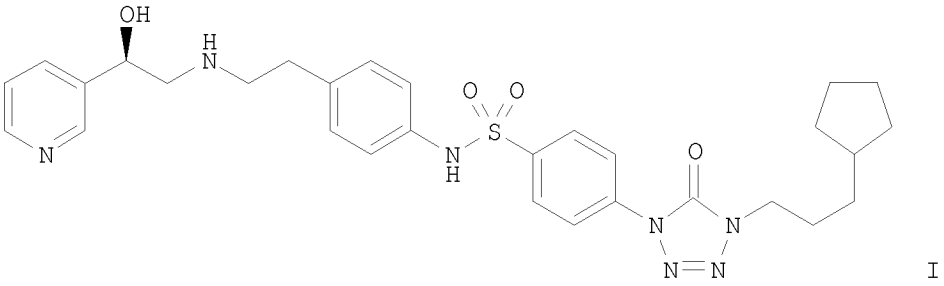
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(9), 1251-1254
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB L-770,644 (I) is a potent and selective agonist of the human β3 adrenergic receptor (EC50 = 13 nM). It shows good oral bioavailability in both dogs and rats (%F = 27), and is a full agonist for glycerolemia in the rhesus monkey (ED50 = 0.21 mg/kg). Based on its desirable in vitro and in vivo properties, L-770,644 was chosen for further preclin. evaluation.

IT 173901-94-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and activity of L-770,644 and derivs. as β3-adrenoceptor agonists)

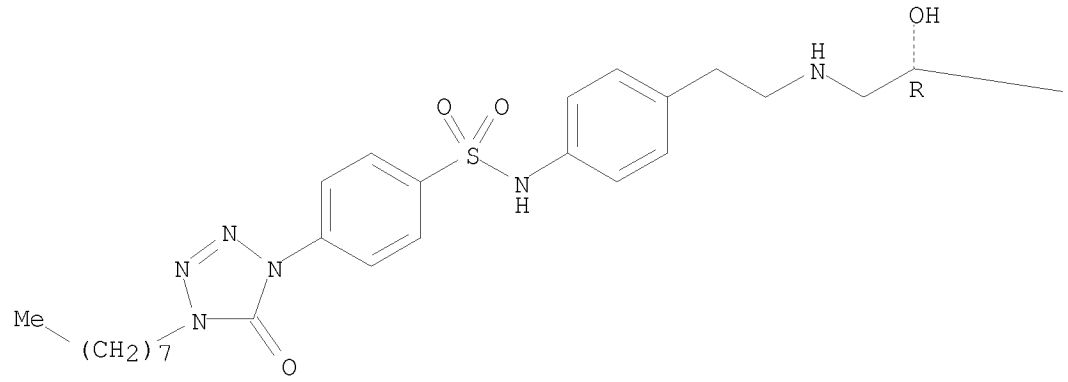
RN 173901-94-5 HCAPLUS

CN Benzenesulfonamide, 4-(4,5-dihydro-4-octyl-5-oxo-1H-tetrazol-1-yl)-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

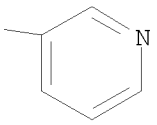
Absolute stereochemistry.

Updated Search

PAGE 1-A



PAGE 1-B



L9 ANSWER 29 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:429288 HCAPLUS
DOCUMENT NUMBER: 131:184913
TITLE: Potent, selective human β3 adrenergic receptor agonists containing a substituted indoline-5-sulfonamide pharmacophore
AUTHOR(S): Mathvink, Robert J.; Barritta, Anna Maria; Candelore, Mari R.; Cascieri, Margaret A.; Deng, Liping; Tota, Laurie; Strader, Catherine D.; Wyvratt, Matthew J.; Fisher, Michael H.; Weber, Ann E.
CORPORATE SOURCE: Departments of Medicinal Chemistry and Biochemistry and Molecular Pharmacology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(13), 1869-1874
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of compds. possessing an N-substituted indoline-5-sulfonamide pharmacophore was prepared and evaluated for their human β3 adrenergic receptor agonist activity. The SAR of a wide range of urea and heterocyclic substituents is discussed. A 4-octylthiazole compound [i.e., (R)-2,3-Dihydro-N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-1-(4-octyl-2-thiazolyl)-1H-indole-5-sulfonamide] was the most potent and selective compound in the series, with 2800-fold selectivity over β1 binding and 1400-fold selectivity over β2 binding.
IT 240140-41-4

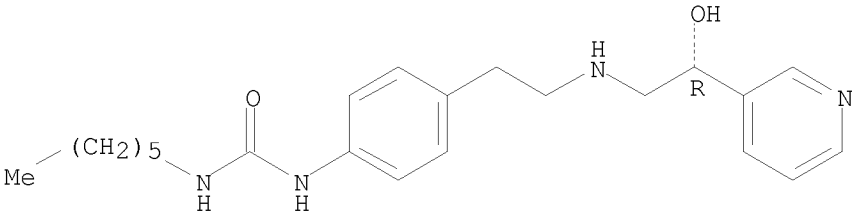
Updated Search

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of selective human β3 adrenergic receptor agonists containing substituted indoline-5-sulfonamide pharmacophore)

RN 240140-41-4 HCAPLUS

CN Urea, N-hexyl-N'-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 30 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:310752 HCAPLUS

DOCUMENT NUMBER: 131:73608

TITLE: L-770,644: a potent and selective human β3 adrenergic receptor agonist with improved oral bioavailability

AUTHOR(S): Shih, Thomas L.; Candelore, Mari R.; Cascieri, Margaret A.; Chiu, Shuet-Hing L.; Colwell, Lawrence F., Jr.; Deng, Liping; Feeney, William P.; Forrest, Michael J.; Hom, Gary J.; MacIntyre, D. Euan; Miller, Randall R.; Stearns, Ralph A.; Strader, Catherine D.; Tota, Laurie; Wyvratt, Matthew J.; Fisher, Michael H.; Weber, Ann E.

CORPORATE SOURCE: Departments of Medicinal Chemistry, Biochemistry & Physiology, Drug Metabolism, Pharmacology and Laboratory Animal Resources, Merck Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(9), 1251-1254
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB L-770,644 [(R)-4-(4-hexyl-4,5-dihydro-5-oxo-1H-tetrazol-1-yl)-N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]benzenesulfonamide] is a potent and selective agonist of the human β3 adrenergic receptor (EC50 = 13 nM). It shows good oral bioavailability in both dogs and rats (%F = 27), and is a full agonist for glycerolemia in the rhesus monkey (ED50 = 0.21 mg/kg). Based on its desirable in vitro and in vivo properties, L-770,644 was chosen for further preclin. evaluation.

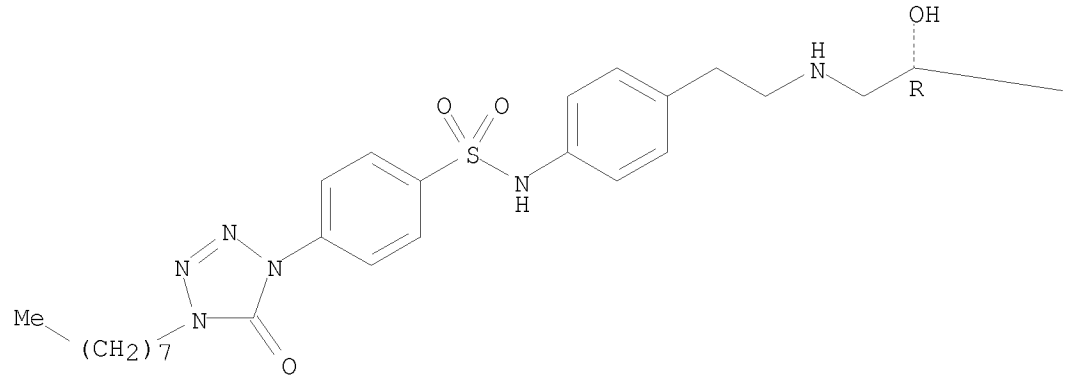
IT 173901-94-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and activity of L-770,644 and derivs. as β3-adrenoceptor

Updated Search

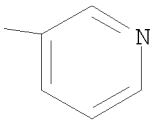
agonists)
RN 173901-94-5 HCAPLUS
CN Benzenesulfonamide, 4-(4,5-dihydro-4-octyl-5-oxo-1H-tetrazol-1-yl)-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 31 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:282201 HCAPLUS
DOCUMENT NUMBER: 130:311793
TITLE: Preparation of amides as antidiabetics
INVENTOR(S): Maruyama, Tatsuya; Suzuki, Takayuki; Onda, Kenichi; Hayakawa, Masahiko; Moritomo, Hiroyuki; Kimizuka, Tetsuya; Matsui, Tetsuo
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920607	A1	19990429	WO 1998-JP4671	19981015 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE,				

Updated Search

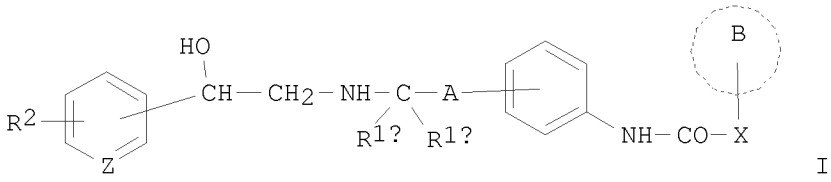
GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI,
SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9889288	A	19990506	AU 1998-89288	19981013	<--
AU 736676	B2	20010802			
CA 2305802	A1	19990429	CA 1998-2305802	19981015	<--
CA 2305802	C	20081118			
AU 9894621	A	19990510	AU 1998-94621	19981015	<--
BR 9804500	A	20000411	BR 1998-4500	19981015	<--
EP 1028111	A1	20000816	EP 1998-947894	19981015	<--
EP 1028111	B1	20040512			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
JP 3193706	B2	20010730	JP 2000-516949	19981015	<--
TW 557295	B	20031011	TW 1998-87117145	19981015	
AT 266639	T	20040515	AT 1998-947894	19981015	
PT 1028111	T	20040930	PT 1998-947894	19981015	
ES 2221204	T3	20041216	ES 1998-947894	19981015	
CN 1218045	A	19990602	CN 1998-121375	19981016	<--
CN 1136192	C	20040128			
HU 9802417	A2	19990830	HU 1998-2417	19981016	<--
HU 9802417	A3	20010730			
RU 2186763	C2	20020810	RU 1998-118906	19981016	
PL 196510	B1	20080131	PL 1998-329233	19981016	
US 6346532	B1	20020212	US 2000-529096	20000407	<--
NO 2000001983	A	20000414	NO 2000-1983	20000414	<--
NO 316673	B1	20040329			

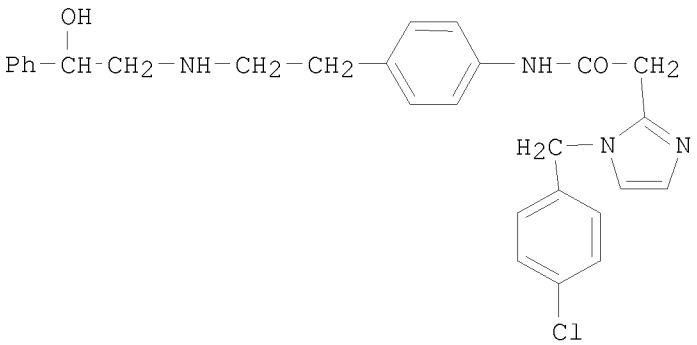
PRIORITY APPLN. INFO.: JP 1997-285778 A 19971017
WO 1998-JP4671 W 19981015

OTHER SOURCE(S): MARPAT 130:311793

GI



I



II

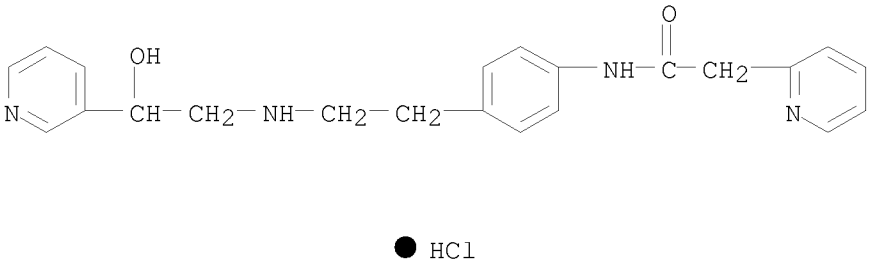
Updated Search

AB The title compds. I [ring B = an optionally substituted heteroaryl optionally fused with a benzene ring; X = a bond, lower alkylene or lower alkenylene (optionally substituted by hydroxy or lower alkyl), carbonyl, or NH (further details related to X are given); A = a lower alkylene or a group represented by (lower alkylene)-O; R1a and R1b = hydrogen or lower alkyl; R2 = hydrogen or halogeno; and Z = nitrogen or CH] are prepared I are useful as diabetes remedies which not only function to accelerate the secretion of insulin and enhance insulin sensitivity but also have an anti-obesity action and an antihyperlipemic action based on their selective stimulative action on β3 receptor. For example, imidazole derivative II was prepared Compds. of this invention significantly decreased blood sugar in mice.

IT 223673-19-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amides as antidiabetics)

RN 223673-19-6 HCAPLUS

CN 2-Pyridineacetamide, N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-, hydrochloride (1:1) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 32 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:193205 HCAPLUS

DOCUMENT NUMBER: 131:27455

TITLE: Human β3 adrenergic receptor agonists containing imidazolidinone and imidazolone benzenesulfonamides

AUTHOR(S): Naylor, Elizabeth M.; Parmee, Emma R.; Colandrea, Vincent J.; Perkins, Leroy; Brockunier, Linda; Candelore, Mari R.; Cascieri, Margaret A.; Colwell, Lawrence F., Jr.; Deng, Liping; Feeney, William P.; Forrest, Michael J.; Hom, Gary J.; MacIntyre, D. Euan; Strader, Catherine D.; Tota, Laurie; Wang, Pei-Ran; Wyvratt, Matthew J.; Fisher, Michael H.; Weber, Ann E.

CORPORATE SOURCE: Departments of Medicinal Chemistry, Molecular Pharmacology/Immunology & Rheumatology, Pharmacology, and Laboratory Animal Resources, Merck Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(5), 755-758
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

Updated Search

LANGUAGE: English

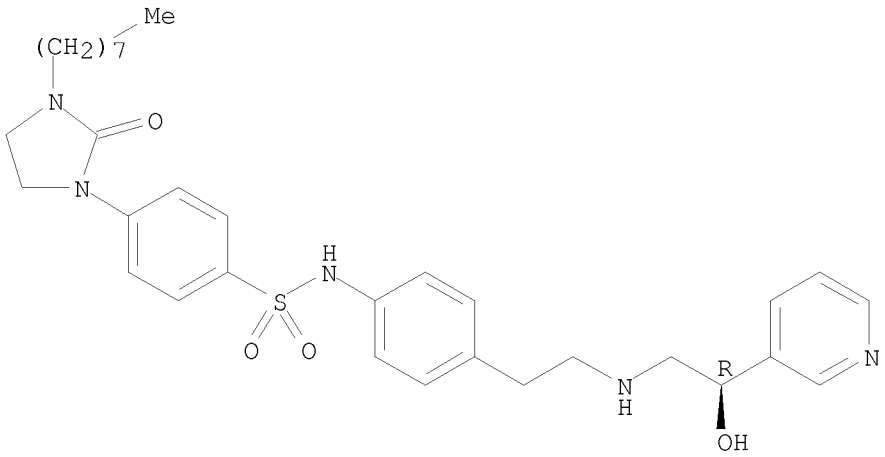
AB Compds. containing imidazolidinone and imidazolone benzenesulfonamides were prepared and tested for β3 adrenergic receptor-agonist activity to find the most potent structure. The cyclopentylpropylimidazolidinone L-766,892 is a potent β3 adrenergic receptor agonist (EC50 5.7 nM, 64% activation) with 420- and 130-fold selectivity over binding to the β1 and β2 adrenergic receptors, resp. In anesthetized rhesus monkeys, L-766,892 elicited dose-dependent lipolytic response (hyperglycerolemia; ED50 0.1 mg/kg) with minimal effects on heart rate.

IT 173901-54-7P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(human β3 adrenergic receptor agonists containing imidazolidinone and imidazolone benzenesulfonamides in relation to lipolytic response and structure)

RN 173901-54-7 HCAPLUS

CN Benzenesulfonamide, N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(3-octyl-2-oxo-1-imidazolidinyl)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 33 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:193204 HCAPLUS

DOCUMENT NUMBER: 131:13357

TITLE: Human β3 adrenergic receptor agonists containing cyclic ureidobenzenesulfonamides

AUTHOR(S): Parmee, Emma R.; Naylor, Elizabeth M.; Perkins, Leroy; Colandrea, Vincent J.; Ok, Hyun O.; Candelore, Mari R.; Cascieri, Margaret A.; Deng, Liping; Feeney, William P.; Forrest, Michael J.; Hom, Gary J.; MacIntyre, D. Euan; Miller, Randall R.; Stearns, Ralph A.; Strader, Catherine D.; Tota, Laurie; Wyvratt, Matthew J.; Fisher, Michael H.; Weber, Ann E.

CORPORATE SOURCE: Departments of Medicinal Chemistry, Molecular

Updated Search

Pharmacology/Immunology and Rheumatology, Pharmacology, Drug Metabolism, and Laboratory Animal Resources, Merck Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(5), 749-754
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 131:13357

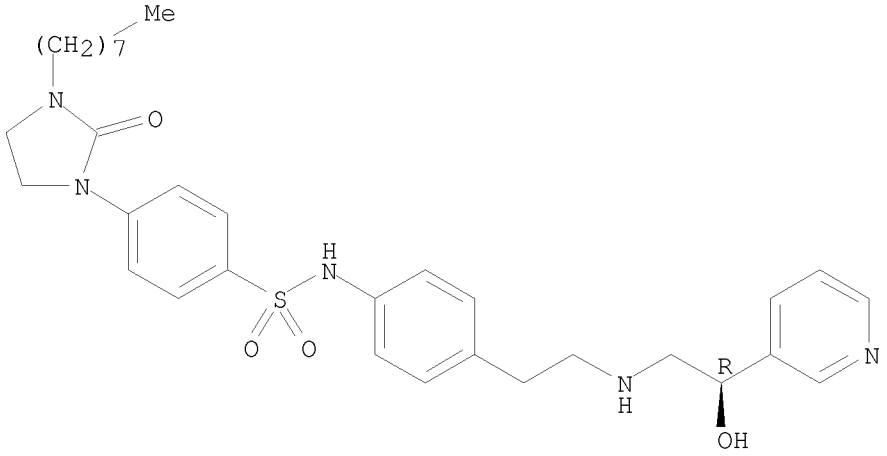
AB Human β3 adrenergic receptor agonists containing 5-membered ring ureas were shown to be potent partial agonists with excellent selectivity over β1 and β2 binding. L-760,087 and L-764,646 (β3 EC50 = 18 and 14 nM, resp.) stimulate lipolysis in rhesus monkeys (ED50 = 0.2 and 0.1 mg/kg, resp.) with minimal effects on heart rate. Oral absorption in dogs is improved over other urea analogs. The results are discussed in relation to treatment of obesity.

IT 173901-54-7P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(human β3 adrenergic receptor agonists containing cyclic ureidobenzenesulfonamides in relation to stimulation of lipolysis and treatment of obesity and oral absorption)

RN 173901-54-7 HCAPLUS

CN Benzenesulfonamide, N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(3-octyl-2-oxo-1-imidazolidinyl)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 34 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:760837 HCAPLUS

DOCUMENT NUMBER: 130:119076

TITLE: 3-Pyridylethanolamines: potent and selective human

Updated Search

β3 adrenergic receptor agonists

AUTHOR(S): Naylor, Elizabeth M.; Colandrea, Vincent J.; Candelore, Mari R.; Cascieri, Margaret A.; Colwell, Lawrence F., Jr.; Deng, Liping; Feeney, William P.; Forrest, Michael J.; Hom, Gary J.; MacIntyre, D. Euan; Strader, Catherine D.; Tota, Laurie; Wang, Pei-Ran; Wyvratt, Matthew J.; Fisher, Michael H.; Weber, Ann E.

CORPORATE SOURCE: Departments of Medicinal Chemistry, Biochemistry and Physiology, Pharmacology, and Laboratory Animal Resources, Merck Research Laboratories, Rahway, NJ, 07065, USA

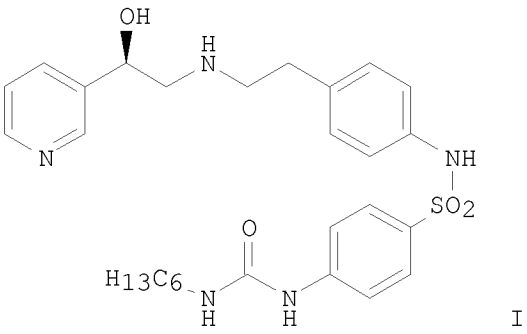
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(21), 3087-3092
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB Of the 3-pyridylethanolamines tested, L-757,793 (I) proved to be a potent β3 AR agonist (EC50 6.3 nM, 70% activation) with 1,300- and 500-fold selectivity over binding to the β1 and β2 ARs, resp. L-757,793 stimulated lipolysis in rhesus monkeys (ED50 0.2 mg/kg) with a maximum response equivalent to that elicited by isoproterenol. Oral bioavailability of L-757,793 was poor; however, the impressive oral bioavailability of the 4-iodobenzensulfonamide suggest that modification of the substituents on the benezenesulfonamide moiety has the potential to produce a compound with the desirable biol. profile of L-757,793, and the pharmacokinetic properties necessary for an oral therapeutic agent.

IT 173901-42-3P, L 757793
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(3-pyridylethanolamines as potent and selective human β3 adrenergic receptor agonists and stimulants of lipolysis)

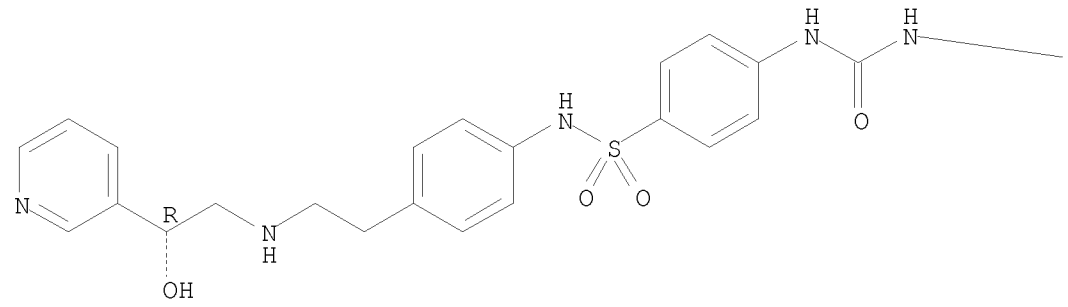
RN 173901-42-3 HCAPLUS

CN Benzenesulfonamide, 4-[[(hexylamino)carbonyl]amino]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

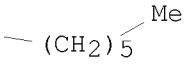
Absolute stereochemistry.

Updated Search

PAGE 1-A



PAGE 1-B

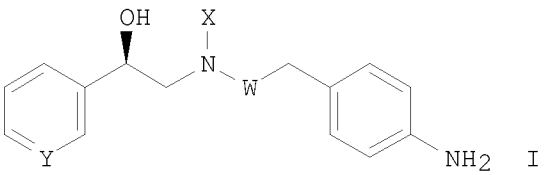


REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 35 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:632236 HCAPLUS
DOCUMENT NUMBER: 129:202860
ORIGINAL REFERENCE NO.: 129:41211a,41214a
TITLE: Preparation of N-Boc-N-(R)-2-((3-pyridyl)-2-hyroxyethyl-N-2-(4-aminophenyl)ethylamine and 2-(4-aminophenyl)-N-2-R-hydroxy-2-pyridine-3-yl-ethyl)acetamide
INVENTOR(S): Zhao, Dalian; Chartrain, Michel M.; Chung, John Y. L.; Roberge, Christopher
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Brit. UK Pat. Appl., 29 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
GB 2315748	A	19980211	GB 1997-14800		19970714 <--
PRIORITY APPLN. INFO.:			US 1996-22056P	P	19960722

OTHER SOURCE(S): CASREACT 129:202860; MARPAT 129:202860
GI



I

Updated Search

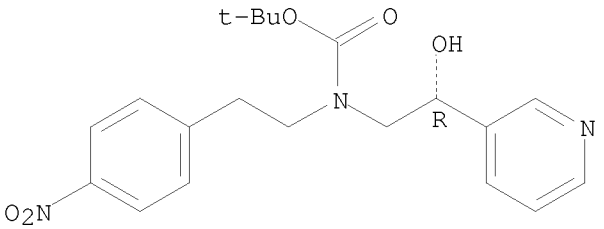
AB The title compds. (I; X = H, Boc; W = CH2, CO; Y = CH, N) are prepared by multi-step reactions from 3-acetylpyridine in an overall good yield. I are useful as intermediates in the production of β-3 agonist for the treatment of obesity and diabetes (no data).

IT 211371-12-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-Boc-N-(R)-2-((3-pyridyl)-2-hyroxyethyl-N-2-(4-aminophenyl)ethylamine and 2-(4-aminophenyl)-N-2-R-hydroxy-2-pyridine-3-yl-ethyl)acetamide)

RN 211371-12-9 HCAPLUS

CN Carbamic acid, [(2R)-2-hydroxy-2-(3-pyridinyl)ethyl][2-(4-nitrophenyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 36 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:542775 HCAPLUS

DOCUMENT NUMBER: 129:175557

ORIGINAL REFERENCE NO.: 129:35681a,35684a

TITLE: Preparation of enantiomeric pyridylethanolamines as pharmaceutical intermediates

INVENTOR(S): Chartrain, Michel M.; Roberge, Christopher; Chung, John Y. L.; Zhao, Dalian

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: U.S., 10 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5792871	A	19980811	US 1997-882977	19970626 <--

PRIORITY APPLN. INFO.: US 1997-882977 19970626

OTHER SOURCE(S): CASREACT 129:175557

AB (R)-R1CH(OH)CH2NRZCH2C6H4(NH2)-4 (R = H and Z = CO or R = CO2CMe3 and Z = CH2; R1 = 3-pyridyl) were prepared by a multistep process including a Neber rearrangement and a yeast asym. reduction

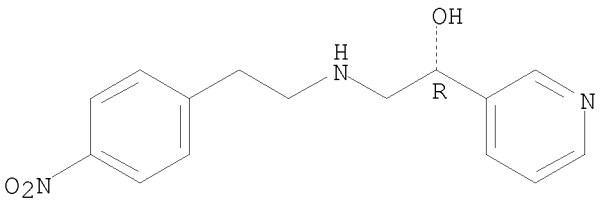
IT 211371-11-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of enantiomeric pyridylethanolamines as pharmaceutical intermediates)

RN 211371-11-8 HCAPLUS

Updated Search

CN 3-Pyridinemethanol, α-[[[2-(4-nitrophenyl)ethyl]amino]methyl]-, hydrochloride (1:2), (αR)- (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 37 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:527330 HCAPLUS
DOCUMENT NUMBER: 129:161557
ORIGINAL REFERENCE NO.: 129:32879a,32882a
TITLE: Thiazole benzenesulfonamides as β3 agonists for the treatment of diabetes and obesity
INVENTOR(S): Mathvink, Robert J.; Parmee, Emma R.; Tolman, Samuel; Weber, Ann E.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

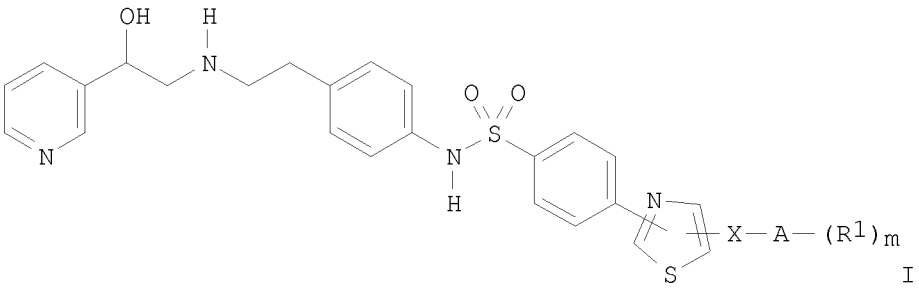
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9832753	A1	19980730	WO 1998-US1317	19980123 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6011048	A	20000104	US 1998-7363	19980115 <--
CA 2278739	A1	19980730	CA 1998-2278739	19980123 <--
AU 9860384	A	19980818	AU 1998-60384	19980123 <--
AU 728812	B2	20010118		
EP 968209	A1	20000105	EP 1998-903677	19980123 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
EE 9900328	A	20000215	EE 1999-328	19980123 <--
BR 9807096	A	20000418	BR 1998-7096	19980123 <--
TR 9902442	T2	20000721	TR 1999-2442	19980123 <--
JP 2001509166	T	20010710	JP 1998-532148	19980123 <--

Updated Search

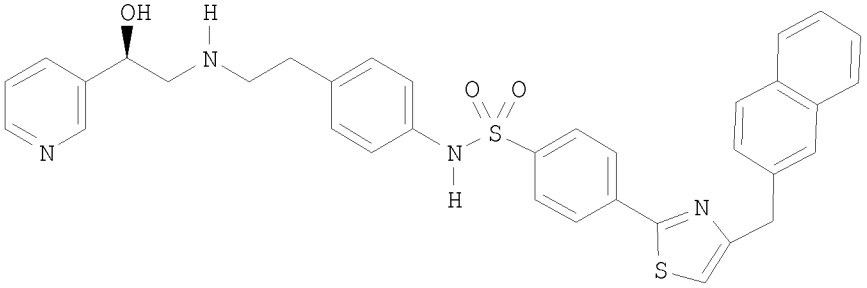
HU 2000002053	A2	20010828	HU 2000-2053		19980123 <--
HU 2000002053	A3	20010928			
ZA 9800647	A	19980728	ZA 1998-647		19980127 <--
NO 9903646	A	19990927	NO 1999-3646		19990727 <--
PRIORITY APPLN. INFO.:			US 1997-36760P	P	19970128
			GB 1997-5041	A	19970312
			WO 1998-US1317	W	19980123

OTHER SOURCE(S): MARPAT 129:161557

GI



I



II

AB Thiazole-substituted benzenesulfonamides I [X = bond, C1-3 alkylene with optional Me or halo substituents or a contained O atom; m = 0-5; A = benzene, heterocycle, benzo-fused carbocycle, or hetero-fused carbo- or heterocycle; R1 = (un)substituted alkyl, cycloalkyl, oxo, halo, cyano, (un)substituted amino, CO2H or esters, etc.] and their prodrugs and pharmaceutically acceptable salts are disclosed. The compds. are β3 adrenergic receptor agonists (no data) with very little β1 and β2 adrenergic receptor activity, and as such are capable of increasing lipolysis and cellular energy expenditure. The compds. thus have potent activity in the treatment of Type II diabetes and obesity. The compds. can also be used to lower triglyceride levels and cholesterol levels or raise high d. lipoprotein levels, or to decrease gut motility. In addition, the compds. can be used to reduce neurogenic inflammation, or as antidepressants. Compns. and methods of use are also disclosed. The compds. are prepared, e.g., by coupling an aminoalkylphenyl-sulfonamide with an appropriately substituted epoxide. Alternatively, for instance, 2-naphthylmethyl chloromethyl ketone was cyclized with 4-bromothiobenzamide to give 2-(4-bromophenyl)-4-(2-naphthylmethyl)thiazole. The latter bromide was lithiated and then treated with SO2 followed by NCS to give the corresponding sulfonyl chloride. Amidation of this with the corresponding enantiomeric amine gave title compound II.

IT 211031-93-5P

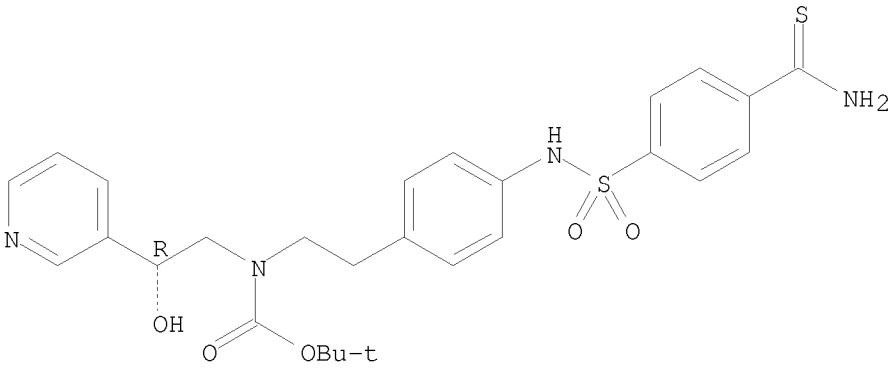
Updated Search

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of thiazole benzenesulfonamides as β3 agonists)

RN 211031-93-5 HCAPLUS

CN Carbamic acid, [2-[4-[[[4-(aminothioxomethyl)phenyl]sulfonyl]amino]phenyl]ethyl][(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 38 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:293388 HCAPLUS

DOCUMENT NUMBER: 129:599

ORIGINAL REFERENCE NO.: 129:151a,154a

TITLE: Combination therapy for the treatment of diabetes and obesity

INVENTOR(S): Smith, Roy G.; Cascieri, Margaret A.; MacIntyre, Euan; MacNeil, Douglas J.; Menke, John G.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818481	A1	19980507	WO 1997-US19880	19971030 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2269660	A1	19980507	CA 1997-2269660	19971030 <--
AU 9851606	A	19980522	AU 1998-51606	19971030 <--
AU 723879	B2	20000907		

Updated Search

US 5908830	A	19990601	US 1997-961749		19971030 <--
EP 969852	A1	20000112	EP 1997-946442		19971030 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
JP 2002516605	T	20020604	JP 1998-520803		19971030 <--
PRIORITY APPLN. INFO.:			US 1996-29233P	P	19961031
			GB 1997-11042	A	19970529
			WO 1997-US19880	W	19971030

AB The combination of a metabolic rate-modifying agent (e.g., a β3 adrenergic receptor agonist) and a feeding behavior modifying agent (e.g., a NPY5 antagonist) is useful in the treatment of obesity and diabetes, either as compds., pharmaceutically acceptable salts, or pharmaceutical composition ingredients. Methods of treating obesity and diabetes are also described.

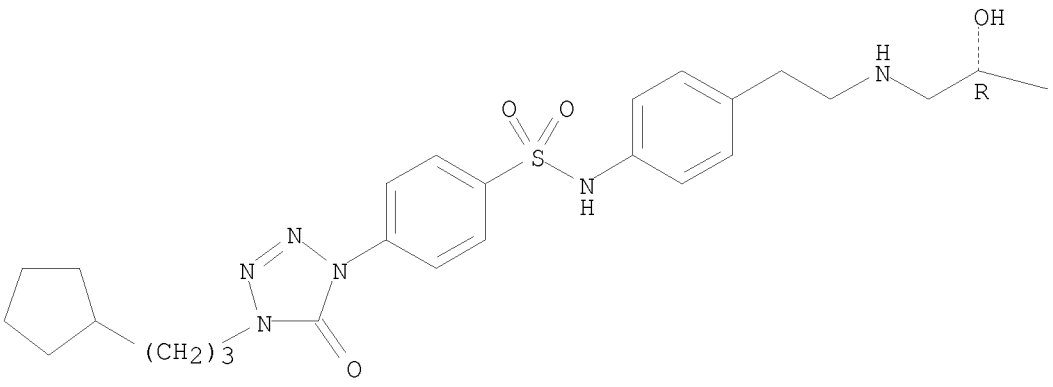
IT 173901-95-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(combination therapy for the treatment of diabetes and obesity)

RN 173901-95-6 HCAPLUS

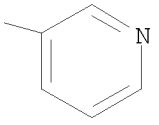
CN Benzenesulfonamide, 4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 39 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:31145 HCAPLUS

Updated Search

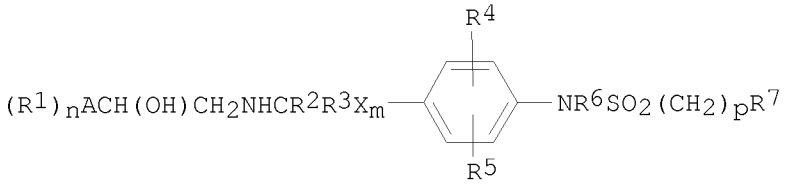
DOCUMENT NUMBER: 128:102082
ORIGINAL REFERENCE NO.: 128:20001a,20004a
TITLE: Preparation of substituted sulfonamides as selective β-3 agonists for the treatment of diabetes and obesity
INVENTOR(S): Fisher, Michael H.; Naylor, Elizabeth M.; Parmee, Emma R.; Shih, Thomas; Ok, Hyun; Weber, Ann E.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 30 pp., Cont.-in-part of U.S. 5,561,142.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5705515	A	19980106	US 1996-684901	19960725 <--
US 5561142	A	19961001	US 1995-445630	19950522 <--
CA 2261167	A1	19980205	CA 1997-2261167	19970721 <--
WO 9804526	A1	19980205	WO 1997-US11999	19970721 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9737232	A	19980220	AU 1997-37232	19970721 <--
EP 915847	A1	19990519	EP 1997-934091	19970721 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000516593	T	20001212	JP 1998-508828	19970721 <--

PRIORITY APPLN. INFO.:

US 1994-233166	B2	19940426
US 1995-404565	B2	19950321
US 1995-445630	A2	19950522
US 1996-684901	A	19960725
WO 1997-US11999	W	19970721

OTHER SOURCE(S): MARPAT 128:102082
GI



I

AB Substituted sulfonamides I [n = 0-5; m = 0, 1; p = 0-3; A = 5- or 6-membered heterocyclic ring or a fused heterocyclic ring; R1 = OH, oxo, halo, cyano, alkyl, etc.; R2, R3 = H, alkyl; X = CH2, CH2CH2, CH:CH, CH2O; R4, R5 = H, alkyl, halo, etc.; R6 = H, alkyl; R7 = Z(R1α)n with R1α = R1, cycloalkyl, substituted Ph, heterocyclyl and Z = Ph, naphthyl, etc.], selective β3 adrenergic receptor agonists with very little β1 and β2 adrenergic receptor activity (no data), were

Updated Search

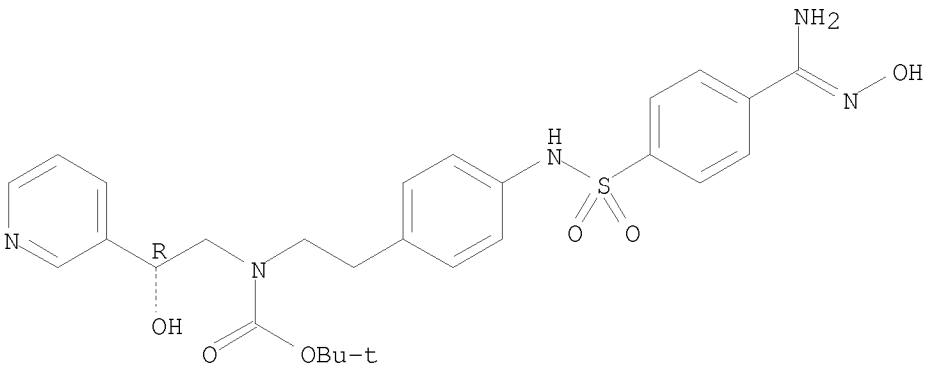
prepared The compds. thus have potent activity in the treatment of Type II diabetes and obesity. The compds. are prepared by coupling an aminoalkylphenyl-sulfonamide with an appropriately substituted epoxide. E.g., reaction of (3-methyl-5-isoxazolyl)oxirane and 4-O2NC6H4CH2CH2NH2, followed by Boc protection, gave N-[2-[4-(aminophenyl)]ethyl]-2-hydroxy-2-(3-methylisoxazol-5-yl)ethylcarbamic acid 1,1-dimethylethyl ester. The latter was reacted with 5-(1-(4-octylthiazol-2-yl)indolinesulfonyl chloride, followed by deprotection, to give N-[4-[2-[[2-hydroxy-2-methylisoxazol-4-yl)ethyl]amino]ethyl]phenyl]-1-(4-octylthiazol-2-yl)-5-indolinesulfonamide.

IT 182251-99-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted sulfonamides as selective β-3 agonists for the treatment of diabetes and obesity)

RN 182251-99-6 HCAPLUS

CN Carbamic acid, [2-[4-[[[4-[(hydroxyamino)iminomethyl]phenyl]sulfonyl]amino]phenyl]ethyl][(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 40 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:1475 HCAPLUS
DOCUMENT NUMBER: 128:75405
ORIGINAL REFERENCE NO.: 128:14751a,14754a
TITLE: Oxadiazole benzenesulfonamides as selective β3 agonists for the treatment of diabetes and obesity
INVENTOR(S): Biftu, Tesfaye; Feng, Danqing Dennis; Fisher, Michael H.; Kuo, Chan-Hwa; Liang, Gui-Bai; Weber, Ann E.; Naylor, Elizabeth M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

Updated Search

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746556	A1	19971211	WO 1997-US9536	19970603 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2257206	A1	19971211	CA 1997-2257206	19970603 <--
AU 9733748	A	19980105	AU 1997-33748	19970603 <--
AU 712057	B2	19991028		
EP 906310	A1	19990407	EP 1997-929769	19970603 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000511903	T	20000912	JP 1998-500782	19970603 <--
US 6034106	A	20000307	US 1997-868556	19970604 <--

PRIORITY APPLN. INFO.:	US 1996-19295P	P	19960607
	GB 1996-14191	A	19960705
	WO 1997-US9536	W	19970603

OTHER SOURCE(S): MARPAT 128:75405
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Oxadiazole-substituted benzenesulfonamides I [X = bond, CO, Q, (un)substituted alkylene; m = 0-5; A = heterocycle, Ph, benzo-fused carbocycle; R1 = (un)substituted alkyl, cycloalkyl, oxo, halo, cyano, (un)substituted amino, groups A, QR2, etc.; R2 = H, (un)substituted alkyl, cycloalkyl, groups A, etc.; Q = NR2, O, S, SO, SO2] and their pharmaceutically acceptable salts are prepared as selective β3 adrenergic receptor agonists, with very little β1 and β2 adrenergic receptor activity (no data). As such, the compds. are capable of increasing lipolysis and energy expenditure in cells. I thus have potent activity in the treatment of type II diabetes and obesity. The compds. can also be used to lower triglyceride and cholesterol levels, raise high-d. lipoprotein levels, or to decrease gut motility. In addition, the compds. can be used to reduce neurogenic inflammation, or as antidepressant agents. The compds. are prepared by coupling (aminoalkyl)phenyl sulfonamides with appropriately substituted epoxides. Compns. and methods for medical use are also disclosed. For instance, (R)-N-[2-(4-aminophenyl)ethyl]-N-[2-hydroxy-2-(pyrid-3-yl)ethyl]carbamic acid 1,1-dimethylethyl ester was subjected to a sequence of sulfonamidation with 4-cyanobenzenesulfonyl chloride, condensation of the nitrile function with NH2OH, cyclocondensation of the resultant aminooximidomethyl group with 4-FC6H4CH2CO2H, and removal of the BOC protective group, to give title compound II.

IT 182251-98-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of oxadiazole benzenesulfonamides as selective β3 adrenergic receptor agonists)

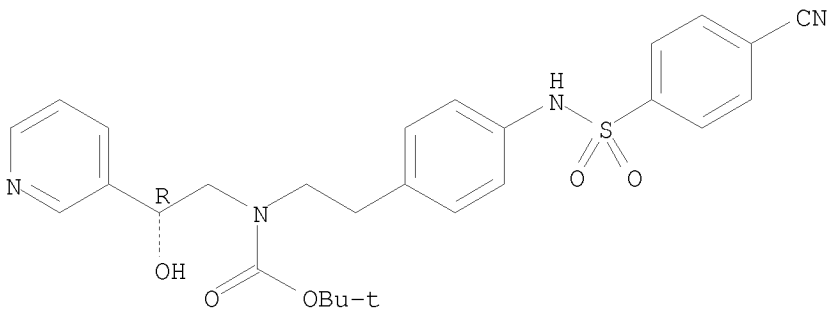
RN 182251-98-5 HCAPLUS

CN Carbamic acid, [2-[4-[[(4-cyanophenyl)sulfonyl]amino]phenyl]ethyl][(2R)-2-

Updated Search

hydroxy-2-(3-pyridinyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 41 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:640652 HCAPLUS
DOCUMENT NUMBER: 127:293230
ORIGINAL REFERENCE NO.: 127:57315a,57318a
TITLE: Process for the preparation of a β3-agonist precursor
INVENTOR(S): Ho, Guo J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Ho, Guo J.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9734880	A1	19970925	WO 1997-US5109		19970314 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU					
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9725536	A	19971010	AU 1997-25536		19970314 <--
PRIORITY APPLN. INFO.:			US 1996-13595P	P	19960318
			GB 1996-10655	A	19960521
			WO 1997-US5109	W	19970314

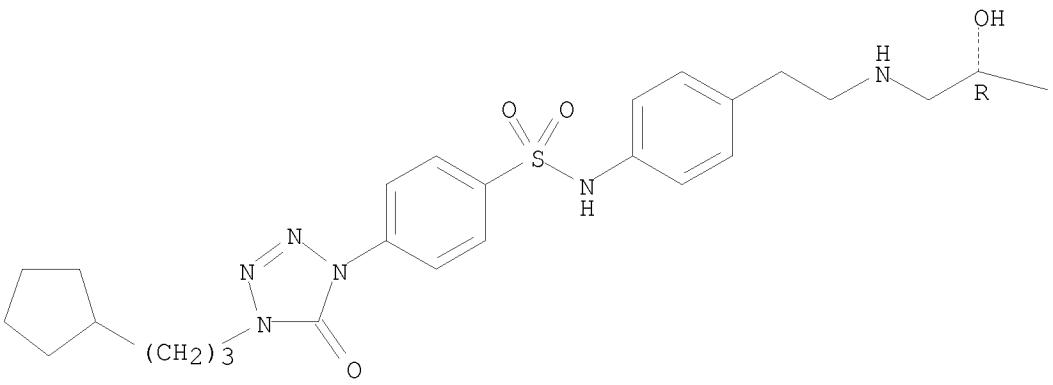
OTHER SOURCE(S): CASREACT 127:293230
AB 3-Cyclopentylpropyl azide, prepared from cyclopentylpropionic acid, and p-chlorosulfonylphenyl isocyanate, prepared from sulfanilic acid and phosgene, undergo cycloaddn. to form 1-(cyclopentylpropyl)-4-(p-chlorosulfonylphenyl)tetrazolin-5-one, a key intermediate in the synthesis of an important β3-agonist. The authors describe potential safety hazards in the process.
IT 173901-95-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic

Updated Search

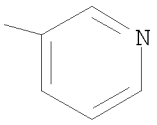
preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (cyclopentylpropyl)(chlorosulfonylphenyl)tetrazolinone)
RN 173901-95-6 HCAPLUS
CN Benzenesulfonamide, 4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 42 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:403174 HCAPLUS
DOCUMENT NUMBER: 127:17682
ORIGINAL REFERENCE NO.: 127:3577a,3580a
TITLE: Preparation of (R)-N-[4-[2-[[2-hydroxy-2-(3-pyridyl)ethyl]amino]ethyl]phenyl]-4-[4-(3-cyclopentylpropyl)-5-oxo-1-tetrazolyl]benzenesulfonamide as a β3 adrenoceptor agonists
INVENTOR(S): Smith, Roy G.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Smith, Roy G.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Updated Search

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9716189	A1	19970509	WO 1996-US17444	19961031 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9674845	A	19970522	AU 1996-74845	19961031 <--
EP 858340	A1	19980819	EP 1996-937097	19961031 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11515027	T	19991221	JP 1996-517529	19961031 <--
PRIORITY APPLN. INFO.:			US 1995-7138P	P 19951101
			GB 1996-3724	A 19960222
			WO 1996-US17444	W 19961031

AB 4-[4-(3-Cyclopentylpropyl)-5-oxo-1-tetrazolyl]benzenesulfonyl chloride was amidated by (R)-4-(H2N)C6H4CH2CH2N(CO2CMe3)CH2CH(OH)R (R = 3-pyridyl)(prepn each given) to give, after deprotection, the title compound (I). Use of I in combination with leptin for treatment of diabetes and obesity was claimed (no data).

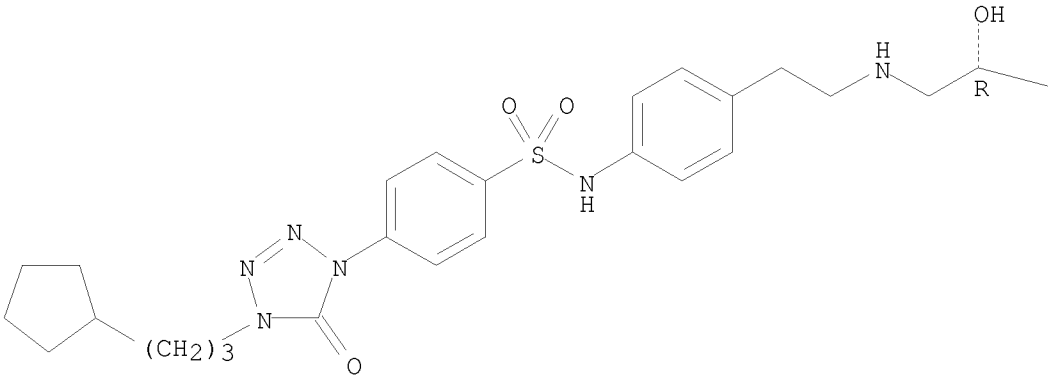
IT 173901-95-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (R)-N-[4-[2-[[2-hydroxy-2-(3-pyridyl)ethyl]amino]ethyl]phenyl]-4-[4-(3-cyclopentylpropyl)-5-oxo-1-tetrazolyl]benzenesulfonamide as a β3 adrenoceptor agonists)

RN 173901-95-6 HCAPLUS

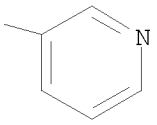
CN Benzenesulfonamide, 4-[4-(3-cyclopentylpropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]-N-[4-[2-[[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



Updated Search

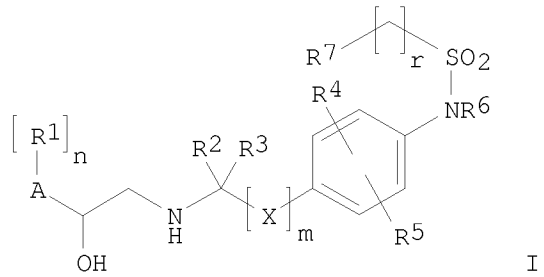


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

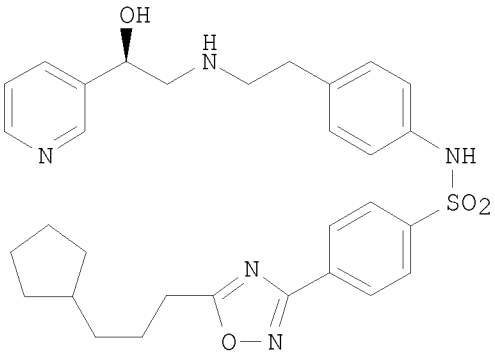
L9 ANSWER 43 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:616601 HCAPLUS
DOCUMENT NUMBER: 125:275666
ORIGINAL REFERENCE NO.: 125:51553a,51556a
TITLE: Preparation of pyridyl-substituted sulfonamides as selective β3 adrenergic receptor agonists for the treatment of type II diabetes and obesity
INVENTOR(S): Fisher, Michael H.; Naylor, Elizabeth M.; Ok, Dong; Weber, Ann E.; Shih, Thomas; Ok, Hyun
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 35 pp., Cont.-in-part of U. S. Ser. No. 404,565, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 5561142	A	19961001	US 1995-445630		19950522	<--
US 5705515	A	19980106	US 1996-684901		19960725	<--
PRIORITY APPLN. INFO.:			US 1994-233166	B2	19940426	
			US 1995-404565	B2	19950321	
			US 1995-445630	A2	19950522	

OTHER SOURCE(S): MARPAT 125:275666
GI



I



II

AB The title compds. [I; A = pyridinyl; R1 = OH, O, halo, etc.; R2, R3 = H, C1-10 alkyl, C1-10 alkoxy, etc.; X = CH2, (CH2)2, CH:CH, CH2O; R4, R5 = H, C1-10 alkyl, halo, etc.; R6 = H, C1-10 alkyl; R7 = (substituted) Ph, naphthyl, a 5- or 6-membered heterocyclic ring, etc.; n = 0-5; m = 0-1; r = 0-3], selective β3 adrenergic receptor agonists and therefore useful in the treatment of type II diabetes and obesity as well as neurogenic inflammation, depression, gastrointestinal disorders, gut motility and as lowering triglyceride and cholesterol levels agents, were prepared by coupling an aminoalkylphenylsulfonamide with an appropriately substituted epoxide. Thus, refluxing (R)-(pyrid-3-yl)oxirane with N-[4-(2-aminoethyl)phenyl]-4-[5-(3-cyclopentylpropyl)[1,2,4]-oxadiazol-3-yl]benzenesulfonamide in dry MeOH afforded the desired product (R)-II. Compds. I were effective at 0.07-350 mg/day when treating diabetes mellitus and/or hyperglycemia.

IT 173901-27-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridyl-substituted sulfonamides as selective β3 adrenergic receptor agonists for the treatment of type II diabetes and obesity)

RN 173901-27-4 HCAPLUS

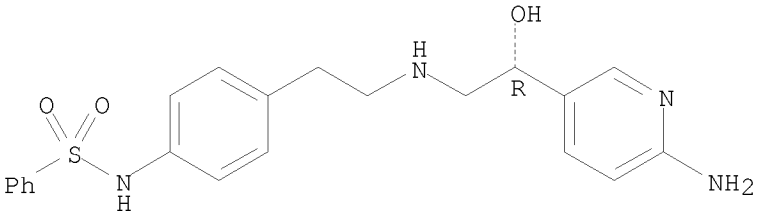
CN Benzenesulfonamide, N-[4-[2-[[2-(6-amino-3-pyridinyl)-2-hydroxyethyl]amino]ethyl]phenyl]-, (R)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 173901-26-3
CMF C21 H24 N4 O3 S

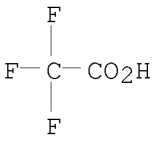
Absolute stereochemistry.

Updated Search



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L9 ANSWER 44 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:494735 HCAPLUS
DOCUMENT NUMBER: 125:221588
ORIGINAL REFERENCE NO.: 125:41417a,41420a
TITLE: Substituted sulfonamides as selective β3 agonists for the treatment of diabetes and obesity
INVENTOR(S): Fisher, Michael H.; Naylor, Elizabeth M.; Weber, Ann E.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 233,166,abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5541197	A	19960730	US 1995-404566	19950321 <--
IL 113410	A	19991130	IL 1995-113410	19950418 <--
CA 2187932	A1	19951102	CA 1995-2187932	19950421 <--
WO 9529159	A1	19951102	WO 1995-US4956	19950421 <--
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9523937	A	19951116	AU 1995-23937	19950421 <--
AU 687558	B2	19980226		
EP 757674	A1	19970212	EP 1995-917116	19950421 <--

Updated Search

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE						
CN 1149869	A	19970514	CN 1995-192821		19950421	<--
HU 76442	A2	19970929	HU 1996-2951		19950421	<--
JP 09512275	T	19971209	JP 1995-527797		19950421	<--
JP 3149186	B2	20010326				
ZA 9503336	A	19960109	ZA 1995-3336		19950425	<--
FI 9604314	A	19961025	FI 1996-4314		19961025	<--
NO 9604548	A	19961223	NO 1996-4548		19961025	<--
PRIORITY APPLN. INFO.:			US 1994-233166	B2	19940426	
			US 1995-404565	A	19950321	
			US 1995-404566	A	19950321	
			WO 1995-US4956	W	19950421	

OTHER SOURCE(S): MARPAT 125:221588
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Substituted sulfonamides I wherein: n is 0-5; m is 0 or 1; p is 0-3; ring A is (1) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (2) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (3) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (4) Ph, or (5) a benzene ring fused to a C3-8 cycloalkyl ring; R1 is, e.g., OH, oxo, halo; R2 and R3 are independently (1) hydrogen, (2) C1-C10 alkyl or (3) C1-C10 alkyl with 1 to 4 substituents selected from hydroxy, C1-C10 alkoxy, and halogen; X is(1) CH2, (2) CH2CH2, (3) CH:CH, or (4) CH2O; R4 and R5 are independently , e.g., hydrogen, C1-C10 alkyl, halogen; R6 is (1) hydrogen or (2) C1-C10 alkyl; R7 is Z-(R1a)n; R1a is, e.g., R1 (with proviso), C3-8 cycloalkyl, optionally substituted Ph; Z is, e.g., Ph, naphthyl, heterocyclic, are selective β3 adrenergic receptor agonists with very little β1 and β2 adrenergic receptor activity and as such the compds. are capable of increasing lipolysis and energy expenditure in cells (no data). The compds. thus have potent activity in the treatment of Type II diabetes and obesity. The compds. can also be used to lower triglyceride levels and cholesterol levels or raise high d. lipoprotein levels or to decrease gut motility. In addition, the compds. can be used to reduced neurogenic inflammation or as antidepressant agents. Compns. and methods for the use of the compds. in the treatment of diabetes and obesity and for lowering triglyceride levels and cholesterol levels or raising high d. lipoprotein levels or for increasing gut motility are also disclosed. Thus, e.g., ring cleavage of (R)-2-(tetrazolo[1,5-a]pyrid-6-yl)oxirane with 2-(4-aminophenyl)ethylamine followed by Boc protection afforded amino alc. II; chlorosulfonylation of N-hexyl-N'-phenylurea (from hexylamine + Ph isocyanate) provided N-hexyl-N'-(4-chlorosulfonylphenyl)urea III; coupling of II + III followed by deprotection afforded sulfonamide IV.

IT 173901-27-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substituted sulfonamides as selective β3 agonists for the treatment of diabetes and obesity)

RN 173901-27-4 HCAPLUS

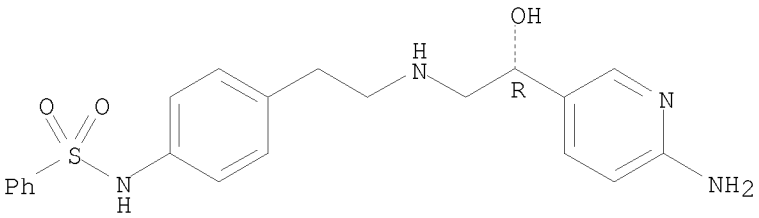
Updated Search

CN Benzenesulfonamide, N-[4-[2-[[2-(6-amino-3-pyridinyl)-2-hydroxyethyl]amino]ethyl]phenyl]-, (R)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

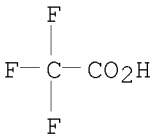
CRN 173901-26-3
CMF C21 H24 N4 O3 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L9 ANSWER 45 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:998182 HCAPLUS
DOCUMENT NUMBER: 124:176115
ORIGINAL REFERENCE NO.: 124:32663a,32666a
TITLE: Preparation of substituted arylsulfonamides as selective β3 agonists for the treatment of diabetes and obesity.
INVENTOR(S): Fisher, Michael H.; Naylor, Elisabeth M.; Ok, Dong; Weber, Ann E.; Shih, Thomas; Ok, Hyun
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9529159	A1	19951102	WO 1995-US4956	19950421 <--

W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG,

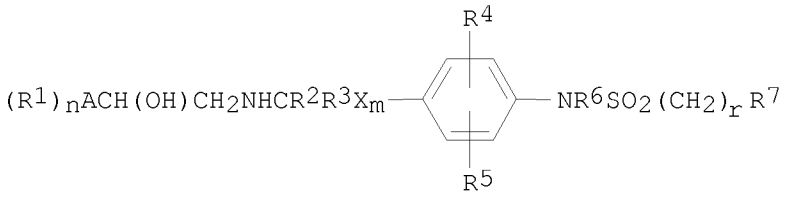
Updated Search

SI, SK, TJ, TT, UA, US, UZ
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

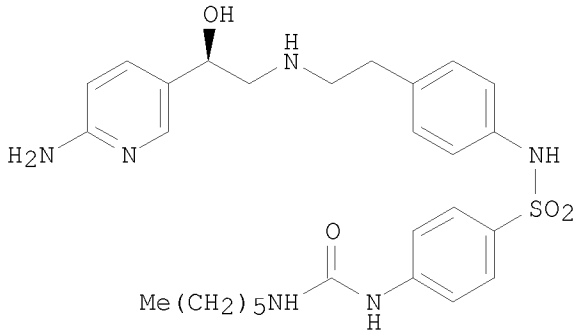
US 5541197	A	19960730	US 1995-404566		19950321 <--
AU 9523937	A	19951116	AU 1995-23937		19950421 <--
AU 687558	B2	19980226			
EP 757674	A1	19970212	EP 1995-917116		19950421 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
JP 09512275	T	19971209	JP 1995-527797		19950421 <--
JP 3149186	B2	20010326			
FI 9604314	A	19961025	FI 1996-4314		19961025 <--
NO 9604548	A	19961223	NO 1996-4548		19961025 <--
PRIORITY APPLN. INFO.:			US 1994-233166	A	19940426
			US 1995-404565	A	19950321
			US 1995-404566	A	19950321
			WO 1995-US4956	W	19950421

OTHER SOURCE(S): MARPAT 124:176115

GI



I



II

AB Title compds. [I; m = 0, 1; n = 0-5; r = 0-3; A = heterocyclyl, benzoheterocyclyl, heterocycloheterocyclyl, Ph, benzocycloalkyl; R1 = OH, O, halo, cyano, amino, CF3, sulfonylamino, (substituted) alkyl, etc.; R2, R3 = H, (substituted) alkyl; R4, R5 = H, alkyl, halo, amino, sulfonylamino, OH, etc; R6 = H, alkyl; R7 = Z(R11)n; R11 = R1, provided that when A = Ph, R11 ≠ alkyl; X = CH2, CH2CH2, CH:CH, CH2O; Z = Ph, naphthyl, heterocyclyl, heterocycloheterocyclyl] were prepared as selective β3 adrenergic receptor agonists with very little β1 and β2 adrenergic receptor activity which are capable of increasing lipolysis and energy expenditure in cells (no data). The compds. thus have potent activity in the treatment of Type II diabetes and obesity. The compds. can also be used to lower triglyceride levels and cholesterol levels or

Updated Search

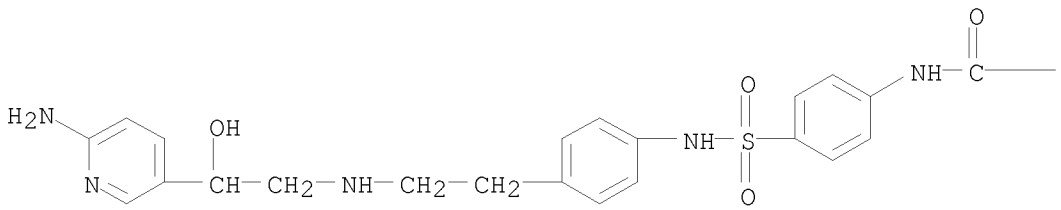
raise high d. lipoprotein levels or to decrease gut motility. In addition, the compds. can be used to reduce neurogenic inflammation or as antidepressant agents. Title compound (II) was prepared in several steps.

IT 173900-63-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted sulfonamides as selective β3 agonists for the treatment of diabetes and obesity)

RN 173900-63-5 HCAPLUS

CN Benzenesulfonamide, N-[4-[2-[[2-(6-amino-3-pyridinyl)-2-hydroxyethyl]amino]ethyl]phenyl]-4-[[(hexylamino)carbonyl]amino]- (CA INDEX NAME)

PAGE 1-A



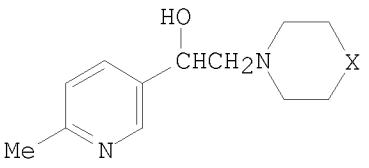
PAGE 1-B

—NH—(CH2)5—Me

L9 ANSWER 46 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1993:118906 HCAPLUS
DOCUMENT NUMBER: 118:118906
ORIGINAL REFERENCE NO.: 118:20529a,20532a
TITLE: Synthesis and pesticidal activity of 2-methyl-5-oxiranylpyridine derivatives
AUTHOR(S): Dryuk, V. G.; Kurochkin, A. F.; Galushkin, S. N.; Kudrya, T. N.; Frantsevich, L. A.; Voitsekhovskaya, O. M.; Shurubura, G. V.; Cherpenyo, T. I.; Panasyuk, A. I.
CORPORATE SOURCE: Inst. Org. Khim., Kiev, Ukraine
SOURCE: Fiziologicheski Aktivnye Veshchestva (1991), 23, 53-8
CODEN: FAVUAI; ISSN: 0533-1153
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI

Updated Search



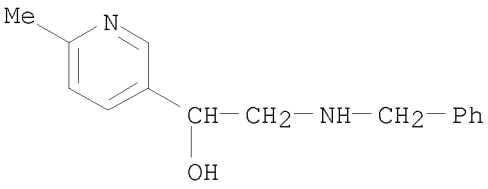
I, X=O
II, X=CH_2

AB Of 11 title compds. , (I) and (II) were most effective in controlling housefly and Schizaphis graminum by >90 and 100% resp., and rice weevil and Leptinotarsa decemlineata by 60-80%. I was also the most effective nematocide, controlling gall nematode by 90%. Acute oral LD50 of I to mice was >300->1000 mg/kg. Synthesis is given.

IT 145908-66-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and insecticidal and nematocidal activity of)

RN 145908-66-3 HCAPLUS

CN 3-Pyridinemethanol, 6-methyl-α-[[(phenylmethyl)amino]methyl]- (CA INDEX NAME)



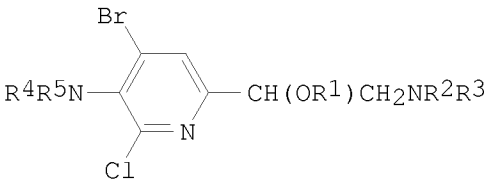
L9 ANSWER 47 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1990:178681 HCAPLUS
DOCUMENT NUMBER: 112:178681
ORIGINAL REFERENCE NO.: 112:30217a,30220a
TITLE: (4-Bromo-6-chloro-5-amino-2-pyridyl)ethanolamines as feed utilization promoters
INVENTOR(S): Lindel, Hans; Hallenbach, Werner; Berschauer, Friedrich; Klotz, Gernot; Greife, Heinrich
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3813839	A1	19891102	DE 1988-3813839	19880423 <--
EP 339345	A2	19891102	EP 1989-106265	19890408 <--
EP 339345	A3	19910327		
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
US 4988694	A	19910129	US 1989-340936	19890420 <--
JP 01313463	A	19891218	JP 1989-100323	19890421 <--
AU 8933342	A	19891026	AU 1989-33342	19890424 <--
AU 616749	B2	19911107		

Updated Search

US 5086181 A 19920204 US 1990-581815 19900913 <--
PRIORITY APPLN. INFO.: DE 1988-3813839 A 19880423
US 1989-340936 A3 19890420
OTHER SOURCE(S): CASREACT 112:178681; MARPAT 112:178681
GI



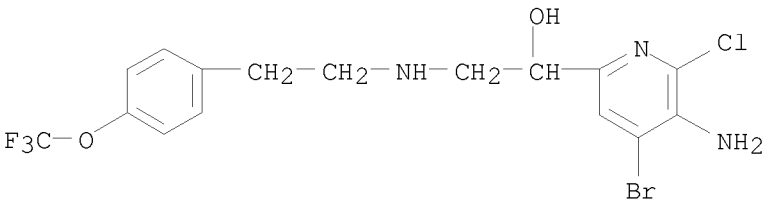
I

AB The title compds. [I; R1 = H, alkyl, acyl, silyl; R2 = H, alkyl; R3 = H, cycloalkyl, (substituted) alkyl, aralkyl, aryl, heterocyclyl; NR2R3 = (substituted) heterocyclyl; R4 = H, alkyl; R5 = H, alkyl, haloalkyl, acyl] and their N-oxides were prepared Thus, 2-chloro-1-(3-amino-4-bromo-2-chloro-6-pyridyl)ethanol and Me3CNH2 in CHCl3 were heated at 100° in an autoclave for 12 h to give 29% I (R1 = R2 = R4 = R5 = H, R3 = Me3C). I at 25 ppm in rat food increased weight gain in female rats to 110-155% of controls.

IT 126552-91-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as feed utilization promoter)

RN 126552-91-8 HCAPLUS

CN 2-Pyridinemethanol, 5-amino-4-bromo-6-chloro-α-[[[2-[4-(trifluoromethoxy)phenyl]ethyl]amino]methyl]- (CA INDEX NAME)



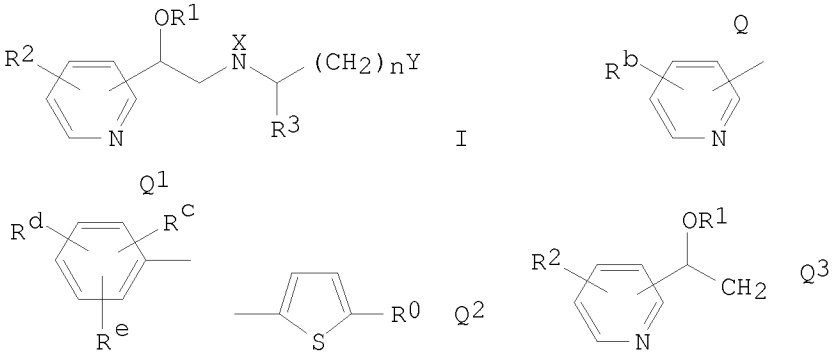
L9 ANSWER 48 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1988:473335 HCAPLUS
DOCUMENT NUMBER: 109:73335
ORIGINAL REFERENCE NO.: 109:12281a,12284a
TITLE: Pyridineethanolamine derivatives, procedure for their preparation, and their use in treating obesity, diabetes mellitus, and increased protein degradation
INVENTOR(S): Alig, Leo; Muller, Marcel
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Updated Search

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
EP 254856	A2	19880203	EP 1987-108706		19870616	<--
EP 254856	A3	19890208				
EP 254856	B1	19910904				
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE						
CA 1287061	C	19910730	CA 1987-538235		19870528	<--
US 4800206	A	19890124	US 1987-57150		19870603	<--
FI 8702589	A	19871228	FI 1987-2589		19870610	<--
AT 66916	T	19910915	AT 1987-108706		19870616	<--
ES 2038619	T3	19930801	ES 1987-108706		19870616	<--
ZA 8704449	A	19880224	ZA 1987-4449		19870619	<--
AU 8774557	A	19880107	AU 1987-74557		19870622	<--
AU 594788	B2	19900315				
IL 82945	A	19910610	IL 1987-82945		19870622	<--
HU 44508	A2	19880328	HU 1987-2860		19870624	<--
HU 198457	B	19891030				
DK 8703295	A	19871228	DK 1987-3295		19870626	<--
DK 166207	B	19930322				
DK 166207	C	19930816				
NO 8702701	A	19871228	NO 1987-2701		19870626	<--
NO 170973	B	19920928				
NO 170973	C	19930106				
JP 63008374	A	19880114	JP 1987-157957		19870626	<--
US 4988714	A	19910129	US 1988-236802		19880826	<--
PRIORITY APPLN. INFO.:			CH 1986-2608	A	19860627	
			CH 1987-1186	A	19870327	
			US 1987-57150	A3	19870603	
			EP 1987-108706	A	19870616	

OTHER SOURCE(S): MARPAT 109:73335

GI



AB Pyridineethanolamines I [n = 1, 2; X = H, alkyl, alkoxyalkyl, CH2CHZORa; Z = Q,Q1, 4-RfC6H4OCH2; Y = 4-RC6H4, Q2; Ro = alkyl, COR4, CR5:CHCOR4; R = Ro, R''; R'' = H, alkyl, alkanoyl, (CH2)1-6OH, (CH2)1-6O(CH2)1-6R6, (CH2)1-6COR4; R1,Ra = alkanoyl, Bz, (CH2)1-6 OH; R2, Rb = H, Cl, Br, CF3; R3,R5 = H, Me; R4 = OH, alkoxy, NR7R8; R6 = H, Rg, OH, COR4; R7,R8 = H, alkyl; Rc,Re = H, Cl, F, Br, CF3; Rd = H, NH2; Rf= H, alkyl; Rc,Re = H, Cl, F, Br, CF3; Rd = H, NH2; Rf= H, AcNH, H2NCOCH2, R9CH2CH2OCH2CH2O;

Updated Search

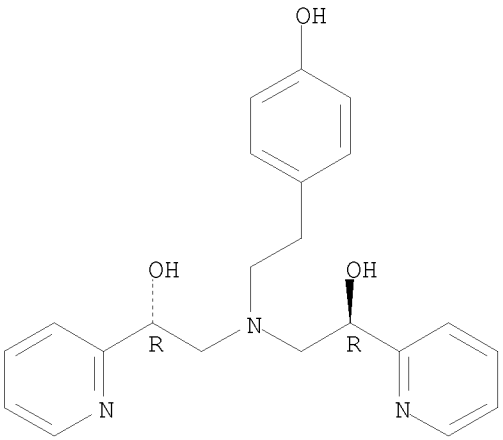
Rg,R9 = Ph (un)substituted with Cl, F, Br], useful in treating obesity, diabetes mellitus, and conditions with elevated protein degradation and as feed additives for fattened animals, were prepared by 2 methods: a) alkylation of X1X2NCHR3(CH2)nY (1 of X1 and X2 = H, the other = X or Q3) with an agent introducing the group Qc or 1 of group X; and b) optionally functionally changing a reactive substituent in a group Y of the reaction product, optionally esterifying an OH β to the amine N atom, and optional conversion of I into a salt. Methylenation of 6-chloro-2-pyridinecarboxaldehyde with Me2S:CH2 gave 2-chloro-6-epoxyethylpyridine which reacted with 4-[(R)-2-aminopropyl]phenol to give α,α'-[[[(R)-4-hydroxy-α-methylphenethyl]imino]dimethylene]bis[(RS)-6-chloro-2-pyridinemethanol] (II) and the corresponding monopyridine compound Treating II with MeSO2OCH2CH2OEt gave the 4-(ethoxyethoxy) analog of II. The latter, at 0.1 μM/kg in rats, gave 165% and 122% O consumption in 1-3 h and 1-12 h, resp., compared with the pre-treatment period O consumption. A formulation comprised (RS)-6-chloro-α-[[[(R)-4-(2-ethoxyethoxy)-α-methylphenethyl]amino]methyl]-2-pyridinemethanol 250, lactose 200, corn starch 300, corn starch paste 50, Ca stearate 5, and Ca phosphate 45 mg.

IT 115548-08-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of obesity, diabetes mellitus, and elevated protein degradation remedy)

RN 115548-08-8 HCAPLUS

CN 2-Pyridinemethanol, α,α'-[[[2-(4-hydroxyphenyl)ethyl]imino]bis(methylene)]bis-, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L9 ANSWER 49 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1988:55893 HCAPLUS
DOCUMENT NUMBER: 108:55893
ORIGINAL REFERENCE NO.: 108:9332h,9333a
TITLE: Ethanolamine derivatives, their preparation, their use as β2-adrenoreceptor stimulators, and

Updated Search

pharmaceutical compositions containing them

INVENTOR(S): Finch, Harry; Lunts, Lawrence Henry Charles; Naylor, Alan; Skidmore, Ian Frederick; Campbell, Ian Baxter; Middlemiss, David; Willbe, Charles

PATENT ASSIGNEE(S): Glaxo Group Ltd., UK

SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 220054	A2	19870429	EP 1986-307974	19861015 <--
EP 220054	A3	19871202		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 62174041	A	19870730	JP 1986-245148	19861015 <--
US 4908386	A	19900313	US 1988-287441	19881220 <--
CN 1048040	A	19901226	CN 1989-104065	19890615 <--

PRIORITY APPLN. INFO.:

GB 1985-25478	A	19851016
GB 1985-25479	A	19851016
GB 1985-25480	A	19851016
GB 1985-25481	A	19851016
GB 1985-25485	A	19851016
US 1986-919123	A1	19861015

OTHER SOURCE(S): MARPAT 108:55893

AB QCH(OH)CH2NHCR1R2XCH2OCH2YAr [I; Ar = (un)substituted Ph; R1, R2 = H, C1-3 alkyl; X = bond, C1-7 alkylene, C2-7 alkenylene, alkynylene; Y = bond, C1-6 alkylene, C2-6 alkylene, alkynylene; Q = 3-substituted 4-HOC6H4, 5-hydroxy-6-(hydroxymethyl)-2-pyridinyl, OH-substituted Ph, optionally substituted by halo] and their physiol. acceptable salts and solvates, useful as β2-adrenoreceptor stimulators (no data), were prepared by 5 methods. A mixture of α-(aminomethyl)-2-phenyl-4H-1,3-dioxino[5,4-b]pyridine-6-methanol and 7-(2-phenylethoxy)-2-heptene was hydrogenated over 5% Pt/C and 10% PdO/C to give α-[[[1-methyl-6-(2-phenylethoxy)hexyl]amino]methyl]-2-phenyl-4H-1,3-dioxino[5,4-b]pyridine-6-methanol which was hydrolyzed with N methanolic HCl and H2O in MeOH 6 h at 50° to give 3-hydroxy-α6-[[[1-methyl-6-(2-phenylethoxy)hexyl]amino]methyl]-2,6-pyridinedimethanol-2HCl. Formulations for I in tablets, pressurized aerosol, and inhalation cartridges were given, e.g., I 2.0, microcryst. cellulose 196.5, and Mg stearate 1.5 mg per tablet.

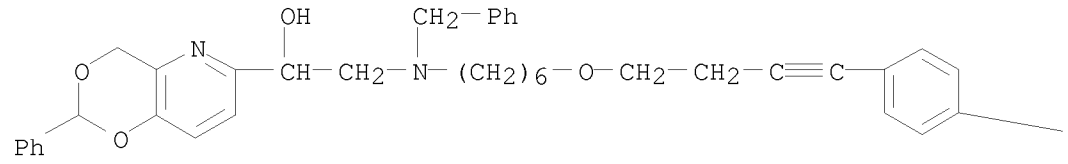
IT 111927-27-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

RN 111927-27-6 HCAPLUS

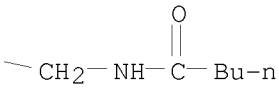
CN Pentanamide, N-[[4-[4-[[6-[[2-hydroxy-2-(2-phenyl-4H-1,3-dioxino[5,4-b]pyridin-6-yl)ethyl](phenylmethyl)amino]hexyl]oxy]-1-butyn-1-yl]phenyl]methyl]- (CA INDEX NAME)

Updated Search

PAGE 1-A



PAGE 1-B

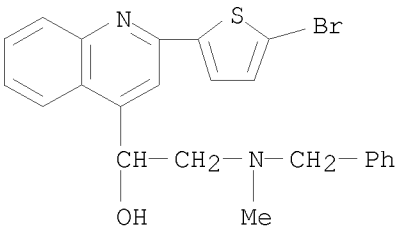


L9 ANSWER 50 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1986:101941 HCAPLUS
DOCUMENT NUMBER: 104:101941
ORIGINAL REFERENCE NO.: 104:15959a,15962a
TITLE: Topological pharmacophores. New methods and their application to a set of antimalarials. Part 2: Results from LOGANA
AUTHOR(S): Franke, Rainer; Streich, W. Juergen
CORPORATE SOURCE: Inst. Drug Res., Ger. Acad. Sci., Berlin, 1136, Ger. Dem. Rep.
SOURCE: Quantitative Structure-Activity Relationships (1985), 4(2), 51-63
CODEN: QSARDI; ISSN: 0722-3676
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The LOGANA procedure is applied to a set of 382 antimalarials as a test case. Its principle consists in the stepwise combination of binary descriptors characterizing the presence or absence of substructural features into conjunctions using the logical operator "and" such that the structural patterns described by these conjunctions are typical of the class of high activity compds. Clear substructural patterns for antimalarial activity are obtained which are consistent with corresponding Hansch equations taken from the literature.

IT 20167-07-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimalarial activity of, topol. anal. of, by computerized methods)
RN 20167-07-1 HCAPLUS
CN 4-Quinolinemethanol, 2-(5-bromo-2-thienyl)-α-[[methyl(phenylmethyl)amino]methyl]- (CA INDEX NAME)

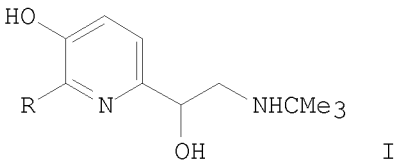
Updated Search



L9 ANSWER 51 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1986:88438 HCAPLUS
DOCUMENT NUMBER: 104:88438
ORIGINAL REFERENCE NO.: 104:14031a
TITLE: 3-Oxypyridine derivatives
INVENTOR(S): Cue, Berkeley Wendell, Jr.; Massett, Stephen Sargent
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Pat. Specif. (Aust.), 34 pp.
CODEN: ALXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AU 544088	B2	19850516	AU 1983-15019	19830526 <--
AU 8315019	A	19830922		
PRIORITY APPLN. INFO.:			AU 1983-15019	19830526

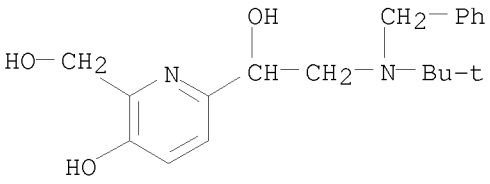
GI



I

AB Title compds. I (R = H, Me, CH2OH) were prepared Thus, treating 5-benzyloxypyridine-2-carboxaldehyde with Me3S+I- and NaOMe in DMF gave 5-benzyloxy-2-(1,2-epoxyethyl)pyridine, amination of which with Me3CNH2 followed by hydroxymethylation with 38% CH2O gave, after treatment with HCl/MeOH, hydrochloride salt of pirbuterol (I, R = CH2OH).HCl.
IT 83881-34-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 83881-34-9 HCAPLUS
CN 2,6-Pyridinedimethanol, α6-[[(1,1-dimethylethyl)(phenylmethyl)amino]methyl]-3-hydroxy-, hydrochloride (1:2) (CA INDEX NAME)

Updated Search

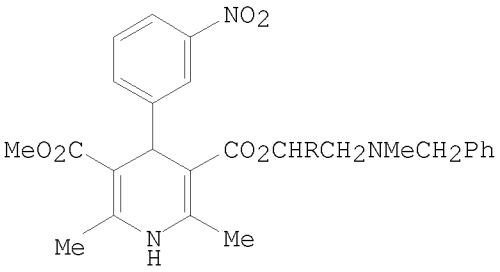


● 2 HCl

L9 ANSWER 52 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1983:215490 HCAPLUS
DOCUMENT NUMBER: 98:215490
ORIGINAL REFERENCE NO.: 98:32765a,32768a
TITLE: 1,4-Dihydropyridine-3,5-dicarboxylic acid esters
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 57200386	A	19821208	JP 1981-86383	19810604 <--
JP 63030911	B	19880621		
CA 1190549	A1	19850716	CA 1982-403487	19820521 <--
EP 68171	A1	19830105	EP 1982-104885	19820603 <--
EP 68171	B1	19851009		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4450165	A	19840522	US 1982-385141	19820604 <--

PRIORITY APPLN. INFO.: JP 1981-86383 A 19810604
OTHER SOURCE(S): MARPAT 98:215490
GI



I

AB Title esters I [R = 2-thienyl (HCl), 3-thienyl (free), 2-furyl (HCl), 2-pyridyl (2HCl), 3-pyridyl (2HCl), 4-pyridyl (2HCl), 1-methyl-3,4-dihydrocarbostyril-6-yl (HCl)] were prepared by, e.g., reaction of MeCOCH2CO2CHRCH2NMeCH2Ph (II), H2NCMe:CHCO2Me (III), and 3-O2NC6H4CHO (IV). Thus, refluxing II (R = 2-thienyl) 18.9, III 6.6, and IV 8.6 g in

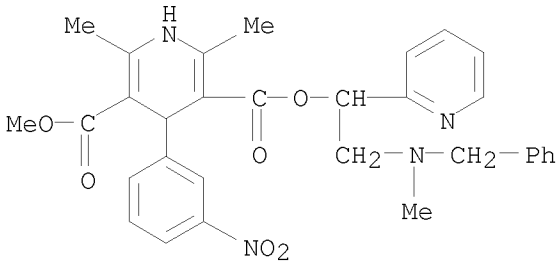
Updated Search

EtOH 16 h gave, after treating with HCl-saturated EtOH, 8 g I.HCl (R = 2-thienyl) (V). Vertebral artery steam enhancing test results of V were shown in dogs.

IT 85892-61-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 85892-61-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 3-methyl 5-[2-[methyl(phenylmethyl)amino]-1-(2-pyridinyl)ethyl] ester, hydrochloride (1:2) (CA INDEX NAME)



●2 HCl

L9 ANSWER 53 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1983:4479 HCAPLUS
DOCUMENT NUMBER: 98:4479
ORIGINAL REFERENCE NO.: 98:801a,804a
TITLE: Process and intermediates for preparing pirbuterol and analogs
INVENTOR(S): Cue, Berkeley Wendell, Jr.; Massett, Stephen Sargent
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 58072	A2	19820818	EP 1982-300605	19820208 <--
EP 58072	A3	19820825		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
SU 1194273	A3	19851123	SU 1982-3392299	19820203 <--
HU 26123	A2	19830928	HU 1982-341	19820204 <--
CS 229678	B2	19840618	CS 1982-781	19820204 <--
FI 8200396	A	19820810	FI 1982-396	19820208 <--
NO 8200371	A	19820810	NO 1982-371	19820208 <--
AU 8280271	A	19820819	AU 1982-80271	19820208 <--
AU 530826	B2	19830728		
DK 8200521	A	19820917	DK 1982-521	19820208 <--
DK 157541	B	19900122		

Updated Search

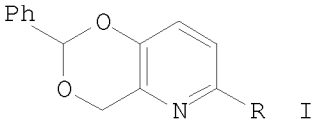
DK 157541	C	19900611			
JP 57150665	A	19820917	JP 1982-18693	19820208	<--
JP 61019624	B	19860517			
ZA 8200778	A	19830126	ZA 1982-778	19820208	<--
DD 202544	A5	19830921	DD 1982-237264	19820208	<--
DD 210034	A5	19840530	DD 1982-253605	19820208	<--
CA 1179677	A1	19841218	CA 1982-395768	19820208	<--
PL 130580	B1	19840831	PL 1982-235000	19820209	<--
PL 130678	B1	19840831	PL 1982-239426	19820209	<--
PL 130917	B1	19840929	PL 1982-239427	19820209	<--
PL 130918	B1	19840929	PL 1982-239428	19820209	<--
IL 64954	A	19860331	IL 1982-64954	19820209	<--
NO 8204273	A	19820810	NO 1982-4273	19821220	<--
NO 8204274	A	19820810	NO 1982-4274	19821220	<--
NO 8204275	A	19820810	NO 1982-4275	19821220	<--
SU 1217253	A3	19860307	SU 1983-3535711	19830105	<--
SU 1240354	A3	19860623	SU 1983-3534107	19830105	<--
SU 1250170	A3	19860807	SU 1983-3534854	19830105	<--
CS 229696	B2	19840618	CS 1983-1072	19830217	<--
CS 229697	B2	19840618	CS 1983-1073	19830217	<--
CS 229698	B2	19840618	CS 1983-1074	19830217	<--
US 4477671	A	19841016	US 1983-500210	19830602	<--
US 4632992	A	19861230	US 1984-641539	19840816	<--
JP 60208964	A	19851021	JP 1985-10723	19850123	<--
JP 60059911	B	19851227			
JP 60208962	A	19851021	JP 1985-10724	19850123	<--
JP 60059231	B	19851224			
JP 61093164	A	19860512	JP 1985-225922	19851009	<--
JP 61035184	B	19860812			
DK 8601809	A	19860421	DK 1986-1809	19860421	<--
FI 8603791	A	19860919	FI 1986-3791	19860919	<--
FI 78075	B	19890228			
FI 78075	C	19890612			
FI 8603792	A	19860919	FI 1986-3792	19860919	<--

PRIORITY APPLN. INFO.:

US 1981-232923	A	19810209
US 1982-340172	A3	19820118
CS 1982-781	A3	19820204
DK 1982-521	A	19820208
FI 1982-396	A	19820208
US 1983-500210	A3	19830602

OTHER SOURCE(S): MARPAT 98:4479

GI



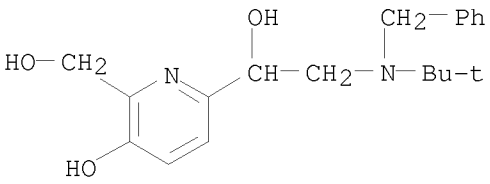
I

AB Pirbuterol was prepared by aminolysis of I (R = epoxyethyl) with Me3CNHCH2Ph, hydrolysis of I [R = CH(OH)CH2N(CH2Ph)CMe3], and debenzylation.

IT 83881-34-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

Updated Search

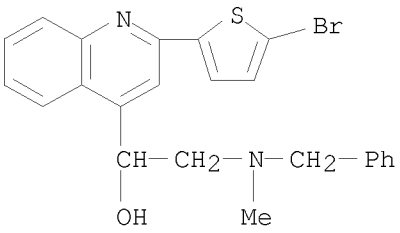
RN 83881-34-9 HCAPLUS
CN 2,6-Pyridinedimethanol, α6-[[(1,1-dimethylethyl)(phenylmethyl)amino]methyl]-3-hydroxy-, hydrochloride (1:2) (CA INDEX NAME)



●2 HCl

L9 ANSWER 54 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1979:161936 HCAPLUS
DOCUMENT NUMBER: 90:161936
ORIGINAL REFERENCE NO.: 90:25591a,25594a
TITLE: Quantitative structure-activity relationships in 1-aryl-2-(alkylamino)ethanol antimalarials
AUTHOR(S): Kim, Ki Hwan; Hansch, Corwin; Fukunaga, James Y.; Steller, Edward E.; Jow, Priscilla Y. C.; Craig, Paul N.; Page, June
CORPORATE SOURCE: Dep. Chem., Pomona Coll., Claremont, CA, USA
SOURCE: Journal of Medicinal Chemistry (1979), 22(4), 366-91
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A quant. structure-activity relation (QSAR) was formulated for 646 arylcarbinol antimalarials (X-ArCHOHCH2NR1R2, having 60 different structures including heterocycles) against Plasmodium berghei, using a equation having 14 terms, 9 of which are indicator variables. The most important determinate of activity was the electron-withdrawing ability of X, whereas the hydrophobic nature of both X and R was less important. The correlation coefficient and the standard deviation for the QSAR were 0.898 and 0.309, resp. An addnl. number of compds. were investigated and the lack of activity of .apprx.100 analogs are discussed.
IT 20167-07-1
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(antimalarial, parameters for predicting activity of)
RN 20167-07-1 HCAPLUS
CN 4-Quinolinemethanol, 2-(5-bromo-2-thienyl)-α-[[methyl(phenylmethyl)amino]methyl]- (CA INDEX NAME)

Updated Search



L9 ANSWER 55 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1973:159437 HCAPLUS
DOCUMENT NUMBER: 78:159437
ORIGINAL REFERENCE NO.: 78:25602h,25603a
TITLE: 1-Phenoxy-3-amino-2-propanol derivatives
INVENTOR(S): Raabe, Thomas; Nitz, Rolf Eberhard; Scholtholt, Josef
PATENT ASSIGNEE(S): Cassella Farbwerke Mainkur A.-G.
SOURCE: Ger. Offen., 41 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2209467	A1	19730215	DE 1972-2209467	19720229 <--
CH 578532	A5	19760813	CH 1971-11415	19710803 <--
CH 582148	A5	19761130	CH 1976-6367	19710803 <--
CH 582149	A5	19761130	CH 1976-6368	19710803 <--
RO 64864	A1	19790115	RO 1972-80406	19720108 <--
NL 7210194	A	19730206	NL 1972-10194	19720724 <--
GB 1362168	A	19740730	GB 1972-34763	19720725 <--
IL 39992	A	19750313	IL 1972-39992	19720725 <--
AU 7244972	A	19740131	AU 1972-44972	19720726 <--
US 3830806	A	19740820	US 1972-276029	19720728 <--
SU 457211	A3	19750115	SU 1972-1816878	19720731 <--
SU 487484	A3	19751005	SU 1972-1971628	19720731 <--
BE 787057	A1	19730201	BE 1972-120533	19720801 <--
PL 93792	B1	19770630	PL 1972-157055	19720801 <--
PL 94261	B1	19770730	PL 1972-181321	19720801 <--
PL 94243	B1	19770730	PL 1972-181323	19720801 <--
PL 94712	B1	19770831	PL 1972-181322	19720801 <--
RO 64865	A1	19790215	RO 1972-80407	19720801 <--
RO 64866	A1	19790215	RO 1972-80408	19720801 <--
FR 2150720	A1	19730413	FR 1972-27840	19720802 <--
ZA 7205316	A	19730530	ZA 1972-5316	19720802 <--
DD 98673	A5	19730712	DD 1972-164829	19720802 <--
AT 323167	B	19750625	AT 1972-6672	19720802 <--
AT 323174	B	19750625	AT 1972-323174	19720802 <--
AT 323175	B	19750625	AT 1972-323175	19720802 <--
AT 323176	B	19750625	AT 1972-323176	19720802 <--
CA 984839	A1	19760302	CA 1972-148527	19720802 <--
HU 165016	B	19740628	HU 1972-CA333	19720803 <--
HU 167906	B	19760128	HU 1972-CA350	19720803 <--
CH 581110	A5	19761029	CH 1973-2094	19730214 <--
CH 581111	A5	19761029	CH 1973-2095	19730214 <--

Updated Search

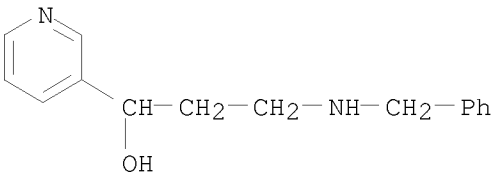
SU 481150	A3	19750815	SU 1973-1971627		19731126 <--
SU 488401	A3	19751015	SU 1973-1971626		19731126 <--
PRIORITY APPLN. INFO.:			CH 1971-11415	A	19710803
			DE 1961-1141571	A	19710803
			DE 1972-2209467	A	19720229

AB ROCH2CH(OH)CH2NHXR1 (R = phenyl, which may be substituted by alkyl, alkoxy, allyl, allyloxy, Ph, Cl, Br, or acylamino groups; X = CH:CHCO, CH2CH2CH(OH); R1 = 2-, 3-, 4-pyridyl) (72 compds.) were prepared Thus 3-acetylpyridine was treated with NaOMe to give the Na salt of 2-nicotinoylvinyl alc., which with o-H2C:CHCH2C6H4OCH2CH(OH)CH2NH2. HCl gave I (X = CH:CHCO). NaBH4 reduction of the latter gave I [X = CH2CH2CH(OH)].

IT 41449-41-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 41449-41-6 HCAPLUS

CN 3-Pyridinemethanol, α-[2-[(phenylmethyl)amino]ethyl]- (CA INDEX NAME)



L9 ANSWER 56 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1972:461749 HCAPLUS
DOCUMENT NUMBER: 77:61749
ORIGINAL REFERENCE NO.: 77:10215a,10218a
TITLE: Synthesis of 1-(4-pyridyl)-2-aminoalkanol dihydrochlorides
AUTHOR(S): Schultz, O. E.; Weber, H.
CORPORATE SOURCE: Pharm. Inst., Univ. Kiel, Kiel, Fed. Rep. Ger.
SOURCE: Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft (1972), 305(4), 248-53
CODEN: APBDAJ; ISSN: 0376-0367
DOCUMENT TYPE: Journal
LANGUAGE: German

GI For diagram(s), see printed CA Issue.

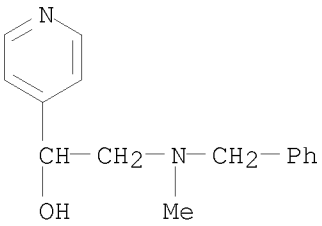
AB Twenty-four title compds. (I, R = H or Me; R1 = H, Me, Et, iso-Pr, 1-pyrrolidinyl; R2 = Me, Et, Pr, Bu, tert-Bu, cyclohexyl, or CH2Ph etc.) were prepared by selective alkylation of I (R1 = R2 = H), by reaction of 4-(bromoacetyl)-pyridines with amines R1NHR2 and reduction of the resulting aminoketones with NaBH4, or by reaction of 1-(4-pyridyl)-2-bromoethanols with amines R1NHR2. I (R = R1 = H, R2 = Pr, iso-, sec-, or tert-Bu) had β-receptor blocking activity.

IT 36696-46-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 36696-46-5 HCAPLUS

CN 4-Pyridinemethanol, α-[[methyl(phenylmethyl)amino]methyl]-, hydrochloride (1:2) (CA INDEX NAME)

Updated Search



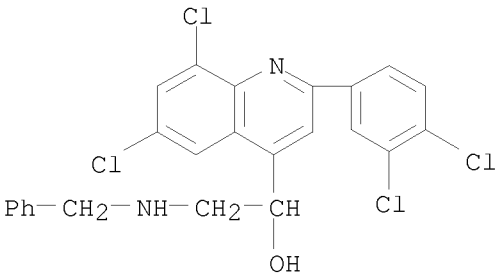
●2 HCl

L9 ANSWER 57 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1972:135536 HCAPLUS
DOCUMENT NUMBER: 76:135536
ORIGINAL REFERENCE NO.: 76:21915a,21918a
TITLE: Structure-activity correlations of antimalarial compounds. 1. Free-Wilson analysis of 2-phenylquinoline-4-carbinols
AUTHOR(S): Craig, Paul N.
CORPORATE SOURCE: Smith Kline and French Lab., Philadelphia, PA, USA
SOURCE: Journal of Medicinal Chemistry (1972), 15(2), 144-9
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sixty-nine 2-phenylquinoline-4-carbinols, which had been tested in the mouse for antimalarial activity, were studied by the Free-Wilson method for structure-activity correlation and the results significantly supported the additivity concept assumed by Free-Wilson. The substituent consts. for groups at the para position of the 2-Ph ring correlated significantly with both Hammett's meta σ consts. and Hansch's π values for those substituents. Substituents on the 7 positon of the quinoline ring correlate well with para σ and π values, and consts. for groups at position 8 correlate with π values for the substituents. Substituent consts. for groups at position 6 and, at the meta position of the 2-Ph ring failed to correlate with σ or π values; the substituent consts. for the 16 different aminoalkyl side chains failed to correlate with π, or π and π2. One may now predict maximum values of log 1/C (C = moles/kg test animal) which might be expected for compds. bearing as yet unstudied substituents.

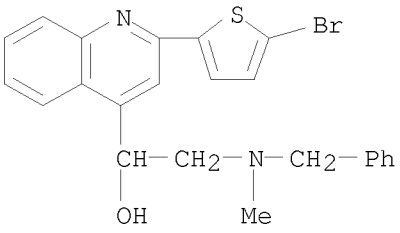
IT 25806-82-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimalarial activity of)
RN 25806-82-0 HCAPLUS
CN 4-Quinolinemethanol, 6,8-dichloro-2-(3,4-dichlorophenyl)-α-[[(phenylmethyl)amino]methyl]- (CA INDEX NAME)

Updated Search



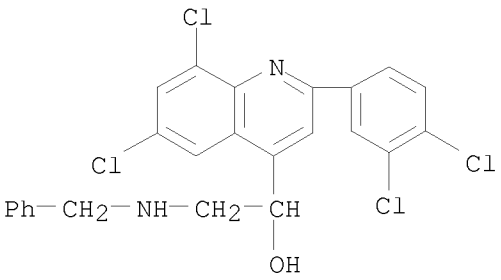
L9 ANSWER 58 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1970:435195 HCAPLUS
DOCUMENT NUMBER: 73:35195
ORIGINAL REFERENCE NO.: 73:5832h,5833a
TITLE: Synthesis of potential antimalarials
AUTHOR(S): Schaefer, John P.; Kulkarni, K. S.; Costin, R.; Higgins, Jerry; Honig, Linda M.
CORPORATE SOURCE: Dep. of Chem., Univ. of Arizona, Tucson, AZ, USA
SOURCE: Journal of Heterocyclic Chemistry (1970), 7(3), 607-13
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 73:35195
AB A series of quinoline derivatives containing a 2-thienyl ring in the 2-position and CO2H, CH2OH, CHO, CH(OH)CN, CH(OH)CO2H, CO2Et, COCH(NEt2)CO2Et, COCH2NEt2, Ac, 2-COC5H4N, and 2-(HO)CHC5H4N substituents in the 4-position was synthesized. Both intermediate and target compounds were tested for antimalarial activity. A second series with a 5-bromo-2-thienyl group in the 2-position and CH(OH)CH2NEt2, CH(OH)CH2Z (Z = piperidino), and CH(OH)CH2N(CH2Ph)2 substituents in the 4-position was also prepared Although these quinolinemethanols were moderately active antimalarials, they exhibited a high degree of phototoxicity. A third series of compds. with 2-alkyl substituents (Me, tert-Bu) was also synthesized; these combined a modest degree of antimalarial activity with low phototoxicity . Several novel synthetic routes to the above compds. were developed and are detailed.
IT 27302-78-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 27302-78-9 HCAPLUS
CN 4-Quinolinemethanol, 2-(5-bromo-2-thienyl)-α-[[methyl(phenylmethyl)amino]methyl]-, hydrochloride (1:2) (CA INDEX NAME)

Updated Search



●2 HCl

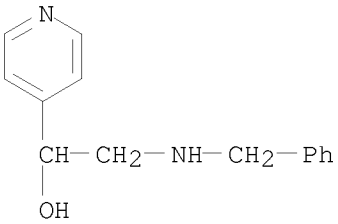
L9 ANSWER 59 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1970:425267 HCAPLUS
DOCUMENT NUMBER: 73:25267
ORIGINAL REFERENCE NO.: 73:4195a,4198a
TITLE: Antimalarials. Quinolinemethanol derivatives
AUTHOR(S): Singh, Tara; Biel, John H.
CORPORATE SOURCE: Res. Lab., Aldrich Chem. Co., Inc., Milwaukee, WI, USA
SOURCE: Journal of Medicinal Chemistry (1970), 13(3), 541
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB I [R = CH(OH)CH2NHCH2Ph] (II) and I (R = 2-(N-benzylaminomethyl)-1,3-dioxolan-2-yl] (III) were prepared from PhCH2NH2 and I (R = 1,2-epoxyethyl) or I [R = 2-(bromomethyl)-1,3-dioxolan-2-yl], resp., and were compared to determine whether the modification of the α-C in R changed the phototoxicity. II showed antimalarial activity against Plasmodium berghei in mice at 40 mg/kg and cured 5 out of 5 mice at 310 mg/kg with no toxic deaths. III was inactive at 640 mg/kg. II was .apprx.9 times as phototoxic as III.
IT 27309-40-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 27309-40-6 HCAPLUS
CN 4-Quinolinemethanol, 6,8-dichloro-2-(3,4-dichlorophenyl)-α-[[(phenylmethyl)amino]methyl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

Updated Search

L9 ANSWER 60 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1964:38677 HCAPLUS
DOCUMENT NUMBER: 60:38677
ORIGINAL REFERENCE NO.: 60:6815a-d
TITLE: Nitrogen-substituted derivatives of 1-(4-pyridyl)-2-aminoethanol
AUTHOR(S): Friz, L. Polo
CORPORATE SOURCE: Lab. Ric. Lab. Bioterapico Milanese Selvi C., Milan
SOURCE: Farmaco, Edizione Scientifica (1963), 18(12), 972-80
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB A series of amino N-substituted derivs. of 1-(4-pyridyl)2-aminoethanol (I) was prepared for pharmacol. comparison with p-nitrophenylaminoethanol. The derivs. of I were prepared in absolute EtOH as follows: 4-Acetylpyridine was treated with Br and 48% HBr to yield 4-(bromoacetyl)pyridine-HBr (II). II was reduced with NaBH4 to 1-(4-pyridyl)-2-bromoethanol-HBr (III.HBr), which was treated with NaHCO3 to give III, which was then treated with the appropriate primary or secondary amine to yield IV. The following IV were prepared (R, R', m.p. di-HCl salt given): H, H, 204° (decomposition); H, Me, 190° (decomposition) (base b0.3 155°, m. 106°); H, Et, 204° (base m. 116°); H, Pr, 183° (base b0.2 163°, m. 63°); H, iso-Pr, 186° (decomposition); H, Bu, 171°; H, sec-Bu, 156°; Me, Me, -- [mono-HCl salt m. 164° (decomposition)]; Et, Et, -- (mono-HCl salt m. 110°); Pr, Pr, 150°; iso-Pr, iso-Pr, 199° (decomposition); Bu, Bu, 53°; H, cyclohexyl, -- (base b2 185°, m. 114°); H, PhCH2, 196° (base m. 101°); (RR'N =) morpholino, 184° (decomposition); (RR'N =) piperidino, 173° (decomposition); (RR'N =) pyrrolidino, 183° (decomposition). Pharmacol. screening of these compds. showed that they were analogous to the p-nitrophenylethanolamines. In particular, the alkyl-substituted derivs. had hypotensive and spasmolytic properties which varied directly with the length of the substituent chain, progressively increasing in going from the Me to the Bu derivative
IT 92255-36-2P, 4-Pyridinemethanol, α-[(benzylamino)methyl]-
RL: PREP (Preparation)
(preparation of)
RN 92255-36-2 HCAPLUS
CN 4-Pyridinemethanol, α-[[(phenylmethyl)amino]methyl]- (CA INDEX NAME)



Updated Search

L9 ANSWER 61 OF 61 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1962:12925 HCAPLUS
DOCUMENT NUMBER: 56:12925
ORIGINAL REFERENCE NO.: 56:2415e-i,2416a-i,2417a-c
TITLE: Syntheses of pyridine derivatives with potential circulatory system action
AUTHOR(S): Zymalkowski, F.; Koppe, F.
CORPORATE SOURCE: Univ. Hamburg, Germany
SOURCE: Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft (1961), 294, 453-68
CODEN: APBDAJ; ISSN: 0376-0367
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 56:12925
AB (Throughout this abstract Z = 3-pyridyl and Y = 3-piperidyl.) ZCH(OH)CH2NH2(I) (3 g.) in 10 ml. absolute EtOH treated with 2.1 ml. 40% CH2O (ice cooling), after 15 min. the mixture (and rinsings with 10 ml. EtOH) added to prehydrogenated 0.15 g. PtO2 in 10 ml. absolute EtOH, hydrogenated 4-5 hrs. at 40°, filtered, the filtrate evaporated in vacuo, and the residue distilled in vacuo gave 67% ZCH(OH)CHRNHCH2R (II) (R = R'= H) (III), b0.4 115-18°; di-HCl salt, very hygroscopic. III (1 g.) in 30 ml. dilute NaOH covered with Et2O, the mixture cooled in ice, treated portionwise with 4.5 g. BzCl, stirred 1 hr. in the ice bath, and stored several days in a refrigerator gave the di-Bz derivative of III, m. 139-41° (1:1 MeOH-H2O). I (3 g.), 30 ml. absolute EtOH, 1.26 g. AcH, and 0.15 g. PtO2. hydrogenated as above (H absorption proceeded in the cold) gave 75% II (R = H, R' = Me) (IV), b0.2 114°; di-HCl salt m. 190-5° (MeOH-Et2O). I (3 g.), 30 ml. absolute EtOH, 3 g. freshly distilled BzH, and 0.15 g. PtO2 hydrogenated as above, after the hydrogenation stopped (20% excess H absorbed) the EtOH evaporated in vacuo, the residue covered with Et2O, acidified with dilute HCl, shaken, the aqueous phase added immediately to excess dilute NaOH, and the product isolated with EtOAc gave II (R = H, R' = Ph), b0.2 189°, m. 81° (EtOAc); di-HCl salt m. 207-9°. Hydrogenation of 3 g. I, 30 ml. absolute EtOH, 1.64 g. EtCHO (V), and 0.15 g. PtO2 gave 61% II (R = H, R' = Et), b0.2 126-8°; di-HCl salt m. 136° (EtOH-Et2O). Hydrogenation of 3 g. ZCH(OH)CH-MeNH2 (VI), 30 ml. EtOH, 2 g. 40% aqueous CH2O, and 0.15 g. PtO2 gave 76% II (R = Me, R' = H), b0.2 115-18°; di-HCl salt m. 222-4°. Hydrogenation of 3 g. VI, 30 ml. absolute EtOH, 1.13 g. AcH, and 0.15 g. PtO2 (after absorption of 0.5 mole H, the hydrogenation became noticeably slower, but it was brought to completion by heating) gave 62% II (R = Me, R' = Me) (Via), b0.14 107-10°; di-HCl salt m. 232-4° (EtOH-Et2O). Hydrogenation of 3 g. VI, 30 ml. absolute EtOH, 2.7 g. freshly distilled BzH, and 0.15 g. PtO2 gave 63% II (R = Me, R' = Ph), b0.19 163°; di-HCl salt m. 210-11°. Hydrogenation of 3 g. VI, 30 ml. absolute EtOH, 1.5 g. V, and 0.15 g. PtO2 gave 76% II (R = Me, R' = Et), b0.34 119-23°; di-HCl salt m. 208-12° (MeOH-Et2O). HOCH2CHO (2 g.) in 12 ml. absolute EtOH refluxed 14 hrs., treated with 3 g. I, and hydrogenated with 0.2 g. PtO2 gave 39% II (R = H, R' = CH2OH) (VII), b0.54 180-5°, m. 90° (EtOH-Et2O); dipicrate m. 172° (H2O). I (5 g.) in 15 ml. absolute EtOH mixed with 16 ml. alc. ethylene oxide (VIII) solu. (1 ml. containing 0.1 g. VIII) under ice-salt cooling, the solution heated 60 hrs. at 40° in a sealed tube, the EtOH evaporated, and the residue distilled in vacuo gave 52% VII. VII (2 g.) heated 7-8 hrs. at 170° with 8-9 g. fuming H2SO4 (20% SO3), the mixture diluted with 20 ml. H2O, neutralized with 40% aqueous NaOH, salted out with K2CO3, percolated

Updated Search

6 hrs. with CHCl3, the extract dried and evaporated, and the residue distilled in vacuo gave 63.5% O.CHZ.-CHR.NH.CH2.CH2 (IX) (R = H), b0.11 98-100°; di-HCl salt m. 212 14° (EtOH-EtOH); dipicrate m. 212° (H2O). VI (5 g.), 15 ml. absolute EtOH, and 14.5 ml. alc. VIII solution heated 70 hrs. at 40° in a sealed tube gave 38% II (R =Me, R' = CH2OH) (X), b0.006 170-5°. Ring closure of X as above gave 50% IX (R = Me), b0.03 106-8°; di-HCl salt m. 235-40° (sublimation). ZCH(OH)CHEtNH2 (XI) (5 g.), 15 ml. absolute EtOH, and 13.25 ml. alc. VIII solution heated 60 hrs. at 60° in a sealed tube gave 31% II (R = Et, R' = CH2OH), b0.01 184-8°, giving (on ring closure, as above) 40% IX (R Et), b0.17 115° [di-HCl salt m. 218-20° (sublimation)]. I (5 g.) treated with 20 g. Ac2O, kept 2 hrs. in a refrigerator and overnight at room temperature, heated 2 hrs. at 100°, and fractionated in vacuo gave 93.5% O, N-di-Ac derivative (XII) of I, b0.4 174-6°; picrate m. 152° (H2O). XII (5 g.) in absolute EtOH hydrogenated with 2.5 g. Pd-BaSO4 catalyst (according to Kuhn) until 1 mole H was absorbed, the catalyst filtered off on a fritted glass funnel, and the filtrate fractionated in vacuo gave 88% ZCH2CHRNHAc (XIII) (R = H), b0.4 157-60°; di-HCl salt m. 145°; dipicrate m. 120° (H2O). XIII (R = H) (3.3 g.) refluxed 15 hrs. in 30 ml. 20% HCl, HCl evaporated in vacuo, the residue made alkaline with 40% aqueous KOH, percolated 3 hrs. with CHCl3, and the extract dried and distilled gave 94% ZCH2CHRNHR' (XIV), (R = R' = H) (XV), b0.7 69-71°; di-HCl salt m. 205° (MeOH). VI (5 g.) treated with 20 g. Ac2O as above gave 84% O,N-di-Ac derivative of VI, b0.4 173°, converted as above to 88% XIII (R = Me), b0.8-0.9 158-61°. Hydrolysis (8 hrs.) of 3 g. XIII (R = Me) with 30 ml. 20% HCl as above gave 78.5% XIV (R = Me, R' = H) (XVI), b0.6 67°; dipicrate m. 178-9° (H2O). XV (1.9 g.), 30 ml. absolute EtOH, and 0.87 g. AcH hydrogenated with 0.2 g. PtO2 gave XIV (R = H, R' = Et) (XVII), b0.6 75°; dipicrate (XVIII) m. 167 8°. IV (3.3 g.) was converted with 15 g. Ac2O to 81% O,N-di-Ac derivative (XIX) of IV, b0.4 156-8°. XIX (3.5 g.) was hydrogenated to 75% ZCH2CH2NEtAc (XX), b0.4 137-40°. Saponification of 1.5 g. XX gave XVII, b0.5 73-4°; XVIII m. 168°. XV (1.9 g.), 30 ml. absolute EtOH, and 2.15 g. freshly distilled BzH hydrogenated with 0.2 g. PtO2 gave 79% XIV (R = H, R' = CH2Ph), b0.4 153-5°; di-HCl salt m. 196°. Hydrogenation of 1 g. XVI, 20 ml. absolute EtOH, and 0.42 g. AcH with 0.2 g. PtO2 gave 75% XIV (R = Me, R' = Et), b0.5-0.6 72-4°; dipicrate m. 150-1° (H2O). XV.2HCl (0.75 g.) in 15 ml. H2O hydrogenated with 50 mg. PtO2 (3 moles H absorbed), the mixture filtered, the filtrate evaporated in vacuo under N, the viscous residue taken up in EtOH, and the solution scratched gave YCH2CHRNHR' (XXI) (R = R' = H) (XXII) di-HCl salt, m. 183°; XXII b0.4 56°. Similarly prepared were quant. XXI (R = Me, R' = H), b0.4 58-62° (di-HCl salt m. 208°), and quant. XXI (R = Et, R' = H) (XXIII), b0.7 81° (di-HCl salt m. 206-7°). XVII (0.8 g.) in 20 ml. N HCl hydrogenated with 0.15 g. PrO2 as above gave XXI (R = H, R' = Et) di-HCl salt, m. 218-19° (EtOHEt2O). Similarly prepared were 86% XXI (R = Me, R' = H), b0.5 68° [dipicrate m. 176°(dilute EtOH)], quant. XXI (R = H, R' = CH2Ph) di-HCl salt, m. 242-3° (sintering from 236°) (EtOH-Et2O), and quant. O.CHY.CH2.NH.CH2.CH2 di-HCl salt, m. 310° (decomposing from 270°) (EtOH containing a little MeOH). PtO2 (0.3 g.) prehydrogenated in 10 ml. H2O, the H2O replaced with AcOH, the suspension mixed with 3 g. I.2HCl in 50 ml. AcOH, shaken with H at room temperature and normal pressure (3.3 moles H absorbed without delay), and filtered, the filtrate evaporated in vacuo under N, the residue made alkaline with 40% aqueous KOH,

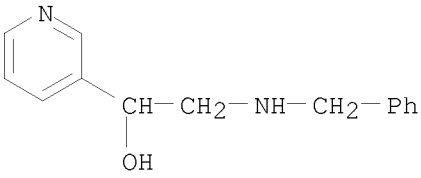
Updated Search

the product salted out with K2CO3, percolated 4 hrs. with CHCl3, the extract dried and evaporated, and the residue distilled in vacuo gave 25% XXII and 52% YCH(OH)CHRNH2 (XXIV) (R = H), b0.4 110-12° (di-HCl salt m. 169-70°). Hydrogenation of 3 g. VI in 50 ml. AcOH with 0.3 g. PtO2 as above gave 15% XVI and 33.5% XXIV (R = Me), b0.4 110-12° [di-HCl salt m. 237° (MeOH-Et2O)]. Similar hydrogenation of 3 g. XI in 50 ml.AcOH with 0.3 g. PtO2 gave 27% XXIII and 51.5% XXIV (R = Et), b0.7 123°. While pharmacol. evaluation of the compds. was still in progress, certain structure-activity relationships were evident. Comparison of the blood pressure action (on decapitated cats) of VI, I, XI, III, VIa, and IV showed that optimal activity was achieved with 3 C atoms in the side chain (VI); alkylation on the N atom decreased the activity (IV had no pressor activity); conversion of I with the side chain of noradrenaline to Via with the side chain of ephedrine (simultaneous methylation on the C and N atoms) produced no change on blood pressure activity, since the methylation effects counterbalanced each other (IV had central nervous system stimulating properties); Via was more active than III or IV; VI was more active than I or XI. The pyridylmorpholines had less activity than I, but the action was more prolonged: IX (R = Me) was more active than IX (R = H), but the activity was lost with the introduction of an Et group [IX (R = Et)]. However, the investigations permitted recognition that structure-activity relationships determined in the benzene series recurred in the pyridine series, and thereby the results confirmed the present conceptions of the spatial prerequisites for the occurrence of a sympathomimetic action.

IT 93045-25-1P, 3-Pyridinemethanol, α-[(benzylamino)methyl]-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

RN 93045-25-1 HCAPLUS

CN 3-Pyridinemethanol, α-[[(phenylmethyl)amino]methyl]-, hydrochloride (1:2) (CA INDEX NAME)



●2 HCl

=>

Updated Search